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(54) Title: SYNTHETIC PEPTIDES AND USES THEREFORE

(57) Abstract: A synthetic polypeptide is disclosed, which comprises a plurality of different segments of at least one parent polypeptide, wherein the segments are linked together in a different relationship relative to their linkage in the at least one parent polypeptide to impede, abrogate or otherwise alter at least one function associated with the parent polypeptide. Synthetic polynucleotides are also disclosed that code for the synthetic polypeptides of the invention as well as expression constructs comprising the synthetic polynucleotides. Also disclosed are methods for constructing the aforementioned molecules and immunopotentiating compositions and methods for treating and/or preventing a disease or condition.

Synthetic Peptides And Uses Therefore.

FIELD OF THE INVENTION

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THIS INVENTION relates generally to agents for modulating immune responses. More particularly, the present invention relates to a synthetic polypeptide comprising a plurality of different segments of a parent polypeptide, wherein the segments are linked to each other such that one or more functions of the parent polypeptide are impeded, abrogated or otherwise altered and such that the synthetic polypeptide, when introduced into a suitable host, can elicit an immune response against the parent polypeptide. The invention also relates to synthetic polynucleotides encoding the synthetic polypeptides and to synthetic constructs comprising these polynucleotides. The invention further relates to the use of the polypeptides and polynucleotides of the invention in compositions for modulating immune responses. The invention also extends to methods of using such compositions for prophylactic and/or therapeutic purposes.

Bibliographic details of various publications referred to in this specification are collected at the end of the description.

BACKGROUND OF THE INVENTION

The modern reductionist approach to vaccine and therapy development has been pursued for a number of decades and attempts to focus only on those parts of pathogens or of cancer proteins which are relevant to the immune system. To date the performance of this approach has been relatively poor considering the vigorous research carried out and the number of effective vaccines and therapies that it has produced. This approach is still being actively pursued, however, despite its poor performance because vaccines developed using this approach are often extremely safe and because only by completely understanding the immune system can new vaccine strategies be developed.

One area that has benefited greatly from research efforts is knowledge about how the adaptive immune system operates and more specifically how T and B cells learn to recognise specific parts of pathogens and cancers. T cells are mainly involved in cell-mediated immunity whereas B cells are involved in the generation of antibody-mediated immunity. The two most important types of T cells involved in adaptive cellular immunity

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are αβ CD8⁺ cytotoxic T lymphocytes (CTL) and CD4⁺ T helper lymphocytes. CTL are important mediators of cellular immunity against many viruses, tumours, some bacteria and some parasites because they are able to kill infected cells directly and secrete various factors which can have powerful effects on the spread of infectious organisms. CTLs recognise epitopes derived from foreign intracellular proteins, which are 8-10 amino acids long and which are presented by class I major histocompatibility complex (MHC) molecules (in humans called human lymphocyte antigens - HLAs) (Jardetzky et al., 1991; Fremont et al., 1992; Rotzschke et al., 1990). T helper cells enhance and regulate CTL responses and are necessary for the establishment of long-lived memory CTL. They also inhibit infectious organisms by secreting cytokines such as IFN-γ. T helper cells recognise epitopes derived mostly from extracellular proteins which are 12-25 amino acids long and which are presented by class II MHC molecules (Chicz et al., 1993; Newcomb et al., 1993). B cells, or more specifically the antibodies they secrete, are important mediators in the control and clearance of mostly extracellular organisms. Antibodies recognise mainly conformational determinants on the surface of organisms, for example, although sometimes they may recognise short linear determinants.

Despite significant advances towards understanding how T and linear B cell epitopes are processed and presented to the immune system, the full potential of epitopebased vaccines has not been fully exploited. The main reason for this is the large number of different T cell epitopes, which have to be included into such vaccines to cover the extreme HLA polymorphism in the human population. The human HLA diversity is one of the main reasons why whole pathogen vaccines frequently provide better population coverage than subunit or peptide-based vaccine strategies. There is a range of epitopebased strategies though which have tried to solve this problem, e.g., peptide blends, peptide conjugates and polyepitope vaccines (ie comprising strings of multiple epitopes) (Dyall et al., 1995; Thomson et al., 1996; Thomson et al., 1998; Thomson et al., 1998). These approaches however will always be sub optimal not only because of the slow pace of epitope characterisation but also, because it is virtually impossible for them to cover every existing HLA polymorphism in the population. A number of strategies have sought to avoid both problems by not identifying epitopes and instead incorporating larger amounts of sequence information e.g., approaches using whole genes or proteins and approaches that mix multiple protein or gene sequences together. The proteins used by these strategies

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however sometimes still function and therefore can compromise vaccine safety e.g., whole cancer proteins. Alternative strategies have tried to improve the safety of vaccines by fragmenting the genes and expressing them either separately or as complex mixtures e.g., library DNA immunisation or by ligating such fragments back together. These approaches are still sub-optimal because they are too complex, generate poor levels of immunity, cannot guarantee that all proteins no longer function and/or that all fragments are present, which compromises substantially complete immunological coverage.

The lack of a safe and efficient vaccine strategy that can provide substantially complete immunological coverage is an important problem, especially when trying to develop vaccines against rapidly mutating and persistent viruses such as HIV and hepatitis C virus, because partial population coverage could allow vaccine-resistant pathogens to reemerge in the future. Human immunodeficiency virus (HIV) is an RNA lentivirus virus approximately 9 kb in length, which infects CD4⁺ T cells, causing T cell decline and AIDS typically 3-8 years after infection. It is currently the most serious human viral infection. evidenced by the number of people currently infected with HIV or who have died from AIDS, estimated by the World Health Organisation (WHO) and UNAIDS in their AIDS epidemic update (December 1999) to be 33.6 and 16.3 million people, respectively. The spread of HIV is also now increasing fastest in areas of the world where over half of the human population reside, hence an effective vaccine is desperately needed to curb the spread of this epidemic. Despite the urgency, an effective vaccine for HIV is still some way off because of delays in defining the correlates of immune protection, lack of a suitable animal model, existence of up to 8 different subtypes of HIV and a high HIV mutation rate.

A significant amount of research has been carried out to try and develop a vaccine capable of generating neutralising antibody responses that can protect against field isolates of HIV. Despite these efforts, it is now clear that the variability, instability and inaccessibility of critical determinants on the HIV envelope protein will make it extremely difficult and perhaps impossible to develop such a vaccine (Kwong *et al.*, 1998). The limited ability of antibodies to block HIV infection is also supported by the observation that development of AIDS correlates primarily with a reduction in CTL responsiveness to HIV and not to altered antibody levels (Ogg *et al.*, 1998). Hence CTL-mediated and not antibody-mediated responses appear to be critical for maintaining the asymptomatic state

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in vivo. There is also some evidence to suggest that pre-existing HIV-specific CTL responses can block the establishment of a latent HIV infection. This evidence comes from a number of cases where individuals have generated HIV-specific CTL responses without becoming infected and appear to be protected from establishing latent HIV infections despite repeated virus exposure (Rowland-Jones et al., 1995; Parmiani 1998). Taken together, these observations suggest that a vaccine capable of generating a broad range of strong CTL responses may be able to stop individuals from becoming latently infected with HIV or at least allow infected individuals to remain asymptomatic for life. Virtually all of the candidate HIV vaccines developed to date have been derived from subtype B HIV proteins (western world subtype) whereas the majority of the HIV infections worldwide are caused by subtypes A/E or C (E and A are similar except in the envelop protein)(referred to as developing world subtypes). Hence existing candidate vaccines may not be suitable for the more common HIV subtypes. Recently, there has been some evidence that B subtype vaccines may be partially effective against other common HIV subtypes (Rowland-Jones et al., 1998). Accordingly, the desirability of a vaccine still remains, whose effectiveness is substantially complete against all isolates of all strains of HIV.

SUMMARY OF THE INVENTION

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The present invention is predicated in part on a novel strategy for enhancing the efficacy of an immunopotentiating composition. This strategy involves utilising the sequence information of a parent polypeptide to produce a synthetic polypeptide that comprises a plurality of different segments of the parent polypeptide, which are linked sequentially together in a different arrangement relative to that of the parent polypeptide. As a result of this change in relationship, the sequence of the linked segments in the synthetic polypeptide is different to a sequence contained within the parent polypeptide. As more fully described hereinafter, the present strategy is used advantageously to cause significant disruption to the structure and/or function of the parent polypeptide while minimising the destruction of potentially useful epitopes encoded by the parent polypeptide.

Thus, in one aspect of the present invention, there is provided a synthetic polypeptide comprising a plurality of different segments of at least one parent polypeptide, wherein the segments are linked together in a different relationship relative to their linkage in the at least one parent polypeptide.

In one embodiment, the synthetic polypeptide consists essentially of different segments of a single parent polypeptide.

In an alternate embodiment, the synthetic polypeptide consists essentially of different segments of a plurality of different parent polypeptides.

Suitably, said segments in said synthetic polypeptide are linked sequentially in a different order or arrangement relative to that of corresponding segments in said at least one parent polypeptide.

Preferably, at least one of said segments comprises partial sequence identity or homology to one or more other said segments. The sequence identity or homology is preferably contained at one or both ends of said at least one segment.

In another aspect, the invention resides in a synthetic polynucleotide encoding the synthetic polypeptide as broadly described above.

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According to yet another aspect, the invention contemplates a synthetic construct comprising a said polynucleotide as broadly described above that is operably linked to a regulatory polynucleotide.

In a further aspect of the invention, there is provided a method for producing a synthetic polynucleotide as broadly described above, comprising:

- linking together in the same reading frame a plurality of nucleic acid sequences encoding different segments of at least one parent polypeptide to form a synthetic polynucleotide whose sequence encodes said segments linked together in a different relationship relative to their linkage in the at least one parent polypeptide.

Preferably, the method further comprises fragmenting the sequence of a respective parent polypeptide into fragments and linking said fragments together in a different relationship relative to their linkage in said parent polypeptide sequence. In a preferred embodiment of this type, the fragments are randomly linked together.

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Suitably, the method further comprises reverse translating the sequence of a respective parent polypeptide or a segment thereof to provide a nucleic acid sequence encoding said parent polypeptide or said segment. In a preferred embodiment of this type, an amino acid of said parent polypeptide sequence is reverse translated to provide a codon, which has higher translational efficiency than other synonymous codons in a cell of interest. Suitably, an amino acid of said parent polypeptide sequence is reverse translated to provide a codon which, in the context of adjacent or local sequence elements, has a lower propensity of forming an undesirable sequence (e.g., a palindromic sequence or a duplicated sequence) that is refractory to the execution of a task (e.g., cloning or sequencing).

In another aspect, the invention encompasses a computer program product for designing the sequence of a synthetic polypeptide as broadly described above, comprising:

- code that receives as input the sequence of at least one parent polypeptide;
- code that fragments the sequence of a respective parent polypeptide into fragments;

- code that links together said fragments in a different relationship relative to their linkage in said parent polypeptide sequence; and
 - a computer readable medium that stores the codes.

In yet another aspect, the invention provides a computer program product for designing the sequence of a synthetic polynucleotide as broadly described above, comprising:

- code that receives as input the sequence of at least one parent polypeptide;
- code that fragments the sequence of a respective parent polypeptide into fragments;
- 10 code that reverse translates the sequence of a respective fragment to provide a nucleic acid sequence encoding said fragment;
 - code that links together in the same reading frame each said nucleic acid sequence to provide a polynucleotide sequence that codes for a polypeptide sequence in which said fragments are linked together in a different relationship relative to their linkage in the at least one parent polypeptide sequence; and
 - a computer readable medium that stores the codes.

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In still yet another aspect, the invention provides a computer for designing the sequence of a synthetic polypeptide as broadly described above, wherein said computer comprises:

- 20 (a) a machine-readable data storage medium comprising a data storage material encoded with machine-readable data, wherein said machine-readable data comprise the sequence of at least one parent polypeptide;
 - (b) a working memory for storing instructions for processing said machine-readable data;
- (c) a central-processing unit coupled to said working memory and to said machinereadable data storage medium, for processing said machine readable data to provide said synthetic polypeptide sequence; and
 - (d) an output hardware coupled to said central processing unit, for receiving said synthetic polypeptide sequence.

In a preferred embodiment, the processing of said machine readable data comprises fragmenting the sequence of a respective parent polypeptide into fragments and linking together said fragments in a different relationship relative to their linkage in the sequence of said parent polypeptide.

In still yet another aspect, the invention resides in a computer for designing the sequence of a synthetic polynucleotide as broadly described above, wherein said computer comprises:

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- (a) a machine-readable data storage medium comprising a data storage material encoded with machine-readable data, wherein said machine-readable data comprise the sequence of at least one parent polypeptide;
- (b) a working memory for storing instructions for processing said machine-readable data;
- (c) a central-processing unit coupled to said working memory and to said machinereadable data storage medium, for processing said machine readable data to provide said synthetic polynucleotide sequence; and
- (d) an output hardware coupled to said central processing unit, for receiving said synthetic polynucleotide sequence.

In a preferred embodiment, the processing of said machine readable data comprises fragmenting the sequence of a respective parent polypeptide into fragments, reverse translating the sequence of a respective fragment to provide a nucleic acid sequence encoding said fragment and linking together in the same reading frame each said nucleic acid sequence to provide a polynucleotide sequence that codes for a polypeptide sequence in which said fragments are linked together in a different relationship relative to their linkage in the at least one parent polypeptide sequence.

According to another aspect, the invention contemplates a composition, comprising an immunopotentiating agent selected from the group consisting of a synthetic polypeptide as broadly described above, a synthetic polynucleotide as broadly described above and a synthetic construct as broadly described above, together with a pharmaceutically acceptable carrier.

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The composition may optionally comprise an adjuvant.

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In a further aspect, the invention encompasses a method for modulating an immune response, which response is preferably directed against a pathogen or a cancer, comprising administering to a patient in need of such treatment an effective amount of an immunopotentiating agent selected from the group consisting of a synthetic polypeptide as broadly described above, a synthetic polynucleotide as broadly described above and a synthetic construct as broadly described above, or a composition as broadly described above.

According to still a further aspect of the invention, there is provided a method for treatment and/or prophylaxis of a disease or condition, comprising administering to a patient in need of such treatment an effective amount of an immunopotentiating agent selected from the group consisting of a synthetic polypeptide as broadly described above, a synthetic polynucleotide as broadly described above and a synthetic construct as broadly described above, or a composition as broadly described above.

The invention also encompasses the use of the synthetic polypeptide, the synthetic polynucleotide and the synthetic construct as broadly described above in the study, and modulation of immune responses.

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BRIEF DESCRIPTION OF THE DRAWINGS

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Figure 1 is a diagrammatic representation showing the number of people living with AIDS in 1998 in various parts of the world and most prevalent HIV clades in these regions. Estimates generated by UNAIDS.

Figure 2 is a graphical representation showing trends in the incidence of the common HIV clades and estimates for the future. Graph from the International Aids Vaccine Initiative (IAVI).

Figure 3 is a diagrammatic representation showing overlapping segments of a parent polypeptide sequence for HIV gag [SEQ ID NO: 1] used for the construction of an embodiment of an HIV Savine. Also shown are the alignments of common HIV clade consensus sequences for the HIV gag protein from the HIV Molecular Immunology Database 1997, Editors Bette Korber, John Moore, Cristian Brander, Richard Koup, Barton Haynes and Bruce Walker. Publisher, Los Alamos National Laboratory, Theoretical Biology and Biophysics, Los Alamos, New Mexico, Pub LAUR 98-485.

Figure 4 is a diagrammatic representation showing overlapping segments of a parent polypeptide sequence for HIV pol [SEQ ID NO: 2] used for the construction of an embodiment of an HIV Savine. Also shown are the alignments of common HIV clade consensus sequences for the HIV pol protein from the HIV Molecular Immunology Database 1997, Editors Bette Korber, John Moore, Cristian Brander, Richard Koup, Barton Haynes and Bruce Walker. Publisher, Los Alamos National Laboratory, Theoretical Biology and Biophysics, Los Alamos, New Mexico, Pub LAUR98-485.

Figure 5 is a diagrammatic representation showing overlapping segments of a parent polypeptide sequence for HIV vif [SEQ ID NO: 3] used for the construction of an embodiment of an HIV Savine. Also shown are the alignments of common HIV clade consensus sequences for the HIV vif protein from the HIV Molecular Immunology Database 1997, Editors Bette Korber, John Moore, Cristian Brander, Richard Koup, Barton Haynes and Bruce Walker. Publisher, Los Alamos National Laboratory, Theoretical Biology and Biophysics, Los Alamos, New Mexico, Pub LAUR98-485.

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Figure 6 is a diagrammatic representation showing overlapping segments of a parent polypeptide sequence for HIV vpr [SEQ ID NO: 4] used for the construction of an embodiment of an HIV Savine. Also shown are the alignments of common HIV clade consensus sequences for the HIV vpr protein from the HIV Molecular Immunology Database 1997, Editors Bette Korber, John Moore, Cristian Brander, Richard Koup, Barton Haynes and Bruce Walker. Publisher, Los Alamos National Laboratory, Theoretical Biology and Biophysics, Los Alamos, New Mexico, Pub LAUR 98-485.

Figure 7 is a diagrammatic representation showing overlapping segments of a parent polypeptide sequence for HIV tat [SEQ ID NO: 5] used for the construction of an embodiment of an HIV Savine. Also shown are the alignments of common HIV clade consensus sequences for the HIV tat protein from the HIV Molecular Immunology Database 1997, Editors Bette Korber, John Moore, Cristian Brander, Richard Koup, Barton Haynes and Bruce Walker. Publisher, Los Alamos National Laboratory, Theoretical Biology and Biophysics, Los Alamos, New Mexico, Pub LAUR 98-485.

Figure 8 is a diagrammatic representation showing overlapping segments of a parent polypeptide sequence for HIV rev [SEQ ID NO: 6] used for the construction of an embodiment of an HIV Savine. Also shown are the alignments of common HIV clade consensus sequences for the HIV rev protein from the HIV Molecular Immunology Database 1997, Editors Bette Korber, John Moore, Cristian Brander, Richard Koup, Barton Haynes and Bruce Walker. Publisher, Los Alamos National Laboratory, Theoretical Biology and Biophysics, Los Alamos, New Mexico, Pub LAUR 98-485.

Figure 9 is a diagrammatic representation showing overlapping segments of a parent polypeptide sequence for HIV vpu [SEQ ID NO: 7] used for the construction of an embodiment of an HIV Savine. Also shown are the alignments of common HIV clade consensus sequences for the HIV vpu protein from the HIV Molecular Immunology Database 1997, Editors Bette Korber, John Moore, Cristian Brander, Richard Koup, Barton Haynes and Bruce Walker. Publisher, Los Alamos National Laboratory, Theoretical Biology and Biophysics, Los Alamos, New Mexico, Pub LAUR 98-485.

Figure 10 is a diagrammatic representation showing overlapping segments of a parent polypeptide sequence for HIV env [SEQ ID NO: 8] used for the construction of an embodiment of an HIV Savine. Also shown are the alignments of common HIV clade

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consensus sequences for the HIV env protein from the HIV Molecular Immunology Database 1997, Editors Bette Korber, John Moore, Cristian Brander, Richard Koup, Barton Haynes and Bruce Walker. Publisher, Los Alamos National Laboratory, Theoretical Biology and Biophysics, Los Alamos, New Mexico, Pub LAUR 98-485.

Figure 11 is a diagrammatic representation showing overlapping segments of a parent polypeptide sequence for HIV nef [SEQ ID NO: 9] used for the construction of an embodiment of an HIV Savine. Also shown are the alignments of common HIV clade consensus sequences for the HIV nef protein from the HIV Molecular Immunology Database 1997, Editors Bette Korber, John Moore, Cristian Brander, Richard Koup, Barton Haynes and Bruce Walker. Publisher, Los Alamos National Laboratory, Theoretical Biology and Biophysics, Los Alamos, New Mexico, Pub LAUR 98-485.

Figure 12 is a diagrammatic representation depicting the systematic segmentation of the designed degenerate consensus sequences for each HIV protein and the reverse translation of each segment into a DNA sequence. Also shown is the number of segments used during random rearrangement and amino acids that were removed. Amino acids surrounded by an open square were removed from the design, because degenerate codons to cater for the desired amino acid combination required too many degenerate bases to comply with the incorporation of degenerate sequence rules outlined in the description of the invention herein. Amino acids surrounded by an open circle were removed only in the segment concerned mainly because they were coded for in an oligonucleotide overlap region. Amino acids marked with an asterisk were designed differently in one fragment compared to the corresponding overlap region (see tat gene)

Figure 13 is a diagrammatic representation showing the first and second most frequently used codons in mammals used to reverse translate HIV protein segments. Also shown are all first and second most frequently used degenerate codons for two amino acids where only one base is varied. Codons used where more than one base was varied were worked out in each case by comparing all the codons for each amino acid. The IUPAC codes for degenerate bases are also shown.

Figure 14 illustrates the construction plan for the HIV Savine showing the approximate sizes of the subcassettes, cassettes and full-length Savine cDNA and the restriction sites involved in joining them together. Also shown are the extra sequences

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added onto each subcassette during their design and a brief description of how the subcassettes, cassettes and full length cDNA were constructed and transferred into appropriate DNA plasmids. Description of full length construction: pA was cleaved with XhoI/SaII and cloned into XhoI arms of the B cassette; pAB was cleaved with XhoI and cloned into XhoI arms of the C cassette; full length construct is excisable with either XbaI/BamHI at the 5' end or BgIII at the 3' end. Options for excising cassettes: A) XbaI/BamHI at the 5' end, BgIII/XhoI at the 3' end; B) XbaI/BamHI at the 5' end, BgIII/SaII at the 3' end. Cleaving plasmid vectors: pDNAVacc is cleavable with XbaI/XhoI (DNA vaccination); pBCB07 or pTK7.5 vectors are cleavable with BamHI/SaII (Recombinant Vaccinia); pAvipox vector pAF09 is cleavable with BamHI/SaII (Recombinant Avipox).

Figure 15 shows the full length DNA (17253 bp) and protein sequence (5742 aas) of the HTV Savine construct. Fragment boundaries are shown, together with the position of each fragment in each designed HTV protein, fragment number (in brackets), spacer residues (two alanine residues) and which fragment the spacer was for (open boxes and arrows). The location of residual restriction site joining sequences corresponding to subcassette or cassette boundaries (shaded boxes) are also shown, along with start and stop codons, Kozak sequence, the location of the murine influenza virus CTL epitope sequence (near the 3' end), important restriction sites at each end and the position of each degenerate amino acid (indicated by 'X').

Figure 16 depicts the layout and position of oligonucleotides in the designed DNA sequence for subcassette A1. The sequences which anneal to the short amplification oligonucleotides are indicated by hatched boxes and the position of oligonucleotide overlap regions are dark shaded.

Figure 17: Panel (a) depicts the stepwise asymmetric PCR of the two halves of subcassette A1 (lanes 2-5 and 7-9, respectively) and final splicing together by SOEing (lane 10). DNA standards in lane 1 are pUC18 digested with Sau3AI. Panel (b) shows the stepwise ligation-mediated joining and PCR amplification of each cassette as indicated. DNA standards in lane 1 are SPP1 cut with EcoRI.

Figure 18: Panel (a) shows summary of the construction of the DNA vaccine plasmids that express one HIV Savine cassette. Panel (b) shows a summary of the

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construction of the plasmids used for marker rescue recombination to generate Vaccinia viruses expressing one HIV Savine cassette. Panel (c) shows a summary of the construction of the DNA vaccine plasmids which each express a version of the full-length HIV Savine cDNA

Figure 19 shows restimulation of HIV specific polyclonal CTL responses from three HIV-infected patients by the HIV Savine constructs. PBMCs from three different patients were restimulated for 7 days by infection with Vaccinia virus pools expressing the HIV Savine cassettes: Pool 1 included VV-AC1 and VV-BC1; Pool 2 included VV-AC2, VV-BC2 and VV-CC2. The restimulated PBMCs were then mixed with autologous LCLs (effector to target ratio of 50:1), which were either uninfected or infected with either Vaccinia viruses expressing the HIV proteins gag (VV-gag), env (VV-env) or pol (VV-pol), VV-HIV Savine pools 1 (light bars) or 2 (dark bars) or a control Vaccinia virus (VV-Lac) and the amount of ⁵¹Cr released used to determine percent specific lysis. K562 cells were used to determine the level of NK cell-mediated killing in their stimulated culture.

Figure 20 is a diagrammatic representation showing CD4+ proliferation of PBMCs from HIV-1 infected patients restimulated with either Pool1 or Pool2 of the HIV-1 Savine. Briefly PBMCs were stained with CFSE and culture for 6 days with or without VVs encoding either pool1 or pool2 of the HIV-1 Savine. Restimulated Cells were then labelled with antibodies and analysed by FACS.

Figure 21 is a graphical representation showing the CTL response in mice vaccinated with the HIV Savine. C57BL6 mice were immunised with the HIV-1 Savine DNA vaccine comprising the six plasmids described in Figure 18a (100 μg total DNA was given as 50 μg/leg i.m.). One week later Poxviruses (1x10⁷ pfu) comprising Pool 1 of the HIV-1 Savine were used to boost the immune responses. Three weeks later splenocytes from these mice were restimulated with VV-Pool 1 or VV-Pool 2 for 5 days and the resultant effectors used in a ⁵¹Cr release cytotoxicity assay against targets infected with CTRVV, VV-pools or VV expressing the natural antigens from HIV-1.

Figure 22 shows immune responses of HIV Immune Macaques (vaccinated with recombinant FPV expressing gag-pol and challenged with HIV-1 2 years prior to experiment). Monkeys 1 and 2 were immunised once at day 0 with VV Savine pool 1 (Three VVs which together express the entire HIV Savine). Monkey 3 was immunised

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twice with FPV-gag-pol *i.e.*, Day 0 is 3 weeks after first FPV-gag-pol immunisation. **A**) IFN-y detection by ELISPOT of whole blood (0.5 mL, venous blood heparinanticoagulated) stimulated with Aldrithiol-2 inactivated whole HIV-1 (20 hours, 20 μg/mL). Plasma samples were then centrifuged (1000xg) and assayed in duplicate for antigen-specific IFN using capture ELISA. **B**) Flow cytometric detection of HIV-1 specific CD69+/CD8+ T cells. Freshly isolated PBMCs were stimulated with inactivated HIV-1 as above for 16 hours, washed and labelled with the antibodies. Cells were then analysed using a FACScaliburTM flow cytometer and data. analysed using Cell-Quest software. **C**) Flow cytometric detection of HIV-1 specific CD69+/CD4+ T cells carried out as in B).

Figure 23 shows a diagram of a system used to carry out the instructions encoded by the storage medium of Figures 28 and 29.

Figure 24 depicts a flow diagram showing an embodiment of a method for designing synthetic polynucleotide and synthetic polypeptides of the invention.

Figure 25 shows an algorithm, which *inter alia* utilises the steps of the method shown in Figure 24.

Figure 26 shows an example of applying the algorithm of Figure 25 to an input consensus polyprotein sequence of Hepatitis C 1a to execute the segmentation of the polyprotein sequence, the rearrangement of the segments, the linkage of the rearranged segments and the outputting of synthetic polynucleotide and polypeptide sequences for the preparation of Savines for treating and/or preventing Hepatitis C infection.

Figure 27 illustrates an example of applying the algorithm of Figure 25 to input consensus melanocyte differentiation antigens (gp100, MART, TRP-1, Tyros, Trp-2, MC1R, MUC1F and MUC1R) and to consensus melanoma specific antigens (BAGE, GAGE-1, gp100In4, MAGE-1, MAGE-3, PRAME, TRP2IN2, NYNSO1a, NYNSO1b and LAGE1) to facilitate segmentation of those sequences, to rearrange the segments, to link the rearranged segments and to synthetic polynucleotide and polypeptide sequences for the preparation of Savines for treating and/or preventing melanoma.

Figure 28 shows a cross section of a magnetic storage medium.

Figure 29 shows a cross section of an optically readable data storage medium.

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Figure 30 shows six HIV Savine cassette sequences (A1 [SEQ ID NO: 393], A2 [SEQ ID NO: 399], B1[SEQ ID NO: 395], B2 [SEQ ID NO: 401], C1 [SEQ ID NO: 397] and C2 [SEQ ID NO: 403]). A1, B1 and C1 can be joined together using, for example, convenient restriction enzyme sites provided at the ends of each cassette to construct an embodiment of a full length HIV Savine [SEQ ID NO: 405]. A2, B2 and C2 can also be joined together to provide another embodiment of a full length HIV Savine with 350 aa mutations common in major HIV clades. The cassettes A/B/C can be joined into single constructs using specific restriction enzyme sites incorporated after the start codon or before the stop codon in the cassettes

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BRIEF DESCRIPTION OF THE SEQUENCES: SUMMARY TABLE

TABLE A

SEQUENCE ID NUMBER	SEQUENCE	<i>LENGTH</i>
SEQ ID NO: 1	GAG consensus polypeptide	499 aa
SEQ ID NO: 2	POL consensus polypeptide	995 aa
SEQ ID NO: 3	VIF consensus polypeptide	192 aa
SEQ ID NO: 4	VPR consensus polypeptide	96 aa
SEQ ID NO: 5	TAT consensus polypeptide	102 aa
SEQ ID NO: 6	REV consensus polypeptide	123 aa
SEQ ID NO: 7	VPU consensus polypeptide	81 aa
SEQ ID NO: 8	ENV consensus polypeptide	651 aa
SEQ ID NO: 9	NEF consensus polypeptide	206 aa
SEQ ID NO: 10	GAG segment 1	90 nts
SEQ ID NO: 11	Polypeptide encoded by SEQ ID NO: 10	30 aa
SEQ ID NO: 12	GAG segment 2	90 nts
SEQ ID NO: 13	Polypeptide encoded by SEQ ID NO: 12	30 aa
SEQ ID NO: 14	GAG segment 3	90 nts
SEQ ID NO: 15	Polypeptide encoded by SEQ ID NO: 14	30 aa
SEQ ID NO: 16	GAG segment 4	90 nts
SEQ ID NO: 17	Polypeptide encoded by SEQ ID NO: 16	30 aa
SEQ ID NO: 18	GAG segment 5	90 nts
SEQ ID NO: 19	Polypeptide encoded by SEQ ID NO: 18	30 aa
SEQ ID NO: 20	GAG segment 6	90 nts
SEQ ID NO: 21	Polypeptide encoded by SEQ ID NO: 20	30 aa
SEQ ID NO: 22	GAG segment 7	90 nts

SEQUENCE ID NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 23	Polypeptide encoded by SEQ ID NO: 22	30 aa
SEQ ID NO: 24	GAG segment 8	90 nts
SEQ ID NO: 25	Polypeptide encoded by SEQ ID NO: 24	30 aa
SEQ ID NO: 26	GAG segment 9	90 nts
SEQ ID NO: 27	Polypeptide encoded by SEQ ID NO: 26	30 aa
SEQ ID NO: 28	GAG segment 10	90 nts
SEQ ID NO: 29	Polypeptide encoded by SEQ ID NO: 28	30 aa
SEQ ID NO: 30	GAG segment 11	90 nts
SEQ ID NO: 31	Polypeptide encoded by SEQ ID NO: 30	30 aa
SEQ ID NO: 32	GAG segment 12	90 nts
SEQ ID NO: 33	Polypeptide encoded by SEQ ID NO: 32	30 aa
SEQ ID NO: 34	GAG segment 13	90 nts
SEQ ID NO: 35	Polypeptide encoded by SEQ ID NO: 34	30 aa
SEQ ID NO: 36	GAG segment 14	90 nts
SEQ ID NO: 37	Polypeptide encoded by SEQ ID NO: 36	30 aa
SEQ ID NO: 38	GAG segment 15	90 nts
SEQ ID NO: 39	Polypeptide encoded by SEQ ID NO: 38	30 aa
SEQ ID NO: 40	GAG segment 16	90 nts
SEQ ID NO: 41	Polypeptide encoded by SEQ ID NO: 40	30 aa
SEQ ID NO: 42	GAG segment 17	90 nts
SEQ ID NO: 43	Polypeptide encoded by SEQ ID NO: 42	30 aa
SEQ ID NO: 44	GAG segment 18	90 nts
SEQ ID NO: 45	Polypeptide encoded by SEQ ID NO: 44	30 aa
SEQ ID NO: 46	GAG segment 19	90 nts

SEQUENCE ID NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 47	Polypeptide encoded by SEQ ID NO: 46	30 aa
SEQ ID NO: 48	GAG segment 20	90 nts
SEQ ID NO: 49	Polypeptide encoded by SEQ ID NO: 48	30 aa
SEQ ID NO: 50	GAG segment 21	90 nts
SEQ ID NO: 51	Polypeptide encoded by SEQ ID NO: 50	30 aa
SEQ ID NO: 52	GAG segment 22	90 nts
SEQ ID NO: 53	Polypeptide encoded by SEQ ID NO: 52	30 aa
SEQ ID NO: 54	GAG segment 23	90 nts
SEQ ID NO: 55	Polypeptide encoded by SEQ ID NO: 54	30 aa
SEQ ID NO: 56	GAG segment 24	90 nts
SEQ ID NO: 57	Polypeptide encoded by SEQ ID NO: 56	30 aa
SEQ ID NO: 58	GAG segment 25	90 nts
SEQ ID NO: 59	Polypeptide encoded by SEQ ID NO: 58	30 aa
SEQ ID NO: 60	GAG segment 26	90 nts
SEQ ID NO: 61	Polypeptide encoded by SEQ ID NO: 60	30 aa
SEQ ID NO: 62	GAG segment 27	90 nts
SEQ ID NO: 63	Polypeptide encoded by SEQ ID NO: 62	30 aa
SEQ ID NO: 64	GAG segment 28	90 nts
SEQ ID NO: 65	Polypeptide encoded by SEQ ID NO: 64	30 aa
SEQ ID NO: 66	GAG segment 29	90 nts
SEQ ID NO: 67	Polypeptide encoded by SEQ ID NO: 66	30 aa
SEQ ID NO: 68	GAG segment 30	90 nts
SEQ ID NO: 69	Polypeptide encoded by SEQ ID NO: 68	30 aa
SEQ ID NO: 70	GAG segment 31	90 nts

SEQUENCE ID NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 71	Polypeptide encoded by SEQ ID NO: 70	30 aa
SEQ ID NO: 72	GAG segment 32	90 nts
SEQ ID NO: 73	Polypeptide encoded by SEQ ID NO: 72	30 aa
SEQ ID NO: 74	GAG segment 33	57 nts
SEQ ID NO: 74		19 aa
	Polypeptide encoded by SEQ ID NO: 74	
SEQ ID NO: 76	POL segment 1	90 nts
SEQ ID NO: 77	Polypeptide encoded by SEQ ID NO: 76	30 aa
SEQ ID NO: 78	POL segment 2	90 nts
SEQ ID NO: 79	Polypeptide encoded by SEQ ID NO: 78	30 aa
SEQ ID NO: 80	POL segment 3	90 nts
SEQ ID NO: 81	Polypeptide encoded by SEQ ID NO: 80	30 aa
SEQ ID NO: 82	POL segment 4	90 nts
SEQ ID NO: 83	Polypeptide encoded by SEQ ID NO: 82	30 aa
SEQ ID NO: 84	POL segment 5	90 nts
SEQ ID NO: 85	Polypeptide encoded by SEQ ID NO: 84	30 aa
SEQ ID NO: 86	POL segment 6	90 nts
SEQ ID NO: 87	Polypeptide encoded by SEQ ID NO: 86	30 aa
SEQ ID NO: 88	POL segment 7	90 nts
SEQ ID NO: 89	Polypeptide encoded by SEQ ID NO: 88	30 aa
SEQ ID NO: 90	POL segment 8	90 nts
SEQ ID NO: 91	Polypeptide encoded by SEQ ID NO: 90	30 aa
SEQ ID NO: 92	POL segment 9	90 nts
SEQ ID NO: 93	Polypeptide encoded by SEQ ID NO: 92	30 aa
SEQ ID NO: 94	POL segment 10	90 nts

SEQUENCE ID NUMBER	SEQUENCE	LENGTH
The state of the s		
SEQ ID NO: 95	Polypeptide encoded by SEQ ID NO: 94	30 aa
SEQ ID NO: 96	POL segment 11	90 nts
SEQ ID NO: 97	Polypeptide encoded by SEQ ID NO: 96	30 aa
SEQ ID NO: 98	POL segment 12	90 nts
SEQ ID NO: 99	Polypeptide encoded by SEQ ID NO: 98	30 aa
SEQ ID NO: 100	POL segment 13	90 nts
SEQ ID NO: 101	Polypeptide encoded by SEQ ID NO: 100	30 aa
SEQ ID NO: 102	POL segment 14	90 nts
SEQ ID NO: 103	Polypeptide encoded by SEQ ID NO: 102	30 aa
SEQ ID NO: 104	POL segment 15	90 nts
SEQ ID NO: 105	Polypeptide encoded by SEQ ID NO: 104	30 aa
SEQ ID NO: 106	POL segment 16	90 nts
SEQ ID NO: 107	Polypeptide encoded by SEQ ID NO: 106	30 aa
SEQ ID NO: 108	POL segment 17	90 nts
SEQ ID NO: 109	Polypeptide encoded by SEQ ID NO: 108	30 aa
SEQ ID NO: 110	POL segment 18	90 nts
SEQ ID NO: 111	Polypeptide encoded by SEQ ID NO: 110	30 aa
SEQ ID NO: 112	POL segment 19	90 nts
SEQ ID NO: 113	Polypeptide encoded by SEQ ID NO: 112	30 aa
SEQ ID NO: 114	POL segment 20	90 nts
SEQ ID NO: 115	Polypeptide encoded by SEQ ID NO: 114	30 aa
SEQ ID NO: 116	POL segment 21	90 nts
SEQ ID NO: 117	Polypeptide encoded by SEQ ID NO: 116	30 aa
SEQ ID NO: 118	POL segment 22	90 nts

SEQUENCE ID NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 119	Polypeptide encoded by SEQ ID NO: 118	30 aa
SEQ ID NO: 120	POL segment 23	90 nts
SEQ ID NO: 121	Polypeptide encoded by SEQ ID NO: 120	30 aa
SEQ ID NO: 122	POL segment 24	90 nts
SEQ ID NO: 123	Polypeptide encoded by SEQ ID NO: 122	30 aa
SEQ ID NO: 124	POL segment 25	90 nts
SEQ ID NO: 125	Polypeptide encoded by SEQ ID NO: 124	30 aa
SEQ ID NO: 126	POL segment 26	90 nts
SEQ ID NO: 127	Polypeptide encoded by SEQ ID NO: 126	30 aa
SEQ ID NO: 128	POL segment 27	90 nts
SEQ ID NO: 129	Polypeptide encoded by SEQ ID NO: 128	30 aa
SEQ ID NO: 130	POL segment 28	90 nts
SEQ ID NO: 131	Polypeptide encoded by SEQ ID NO: 130	30 aa
SEQ ID NO: 132	POL segment 29	90 nts
SEQ ID NO: 133	Polypeptide encoded by SEQ ID NO: 132	30 aa
SEQ ID NO: 134	POL segment 30	90 nts
SEQ ID NO: 135	Polypeptide encoded by SEQ ID NO: 134	30 aa
SEQ ID NO: 136	POL segment 31	90 nts
SEQ ID NO: 137	Polypeptide encoded by SEQ ID NO: 136	30 aa
SEQ ID NO: 138	POL segment 32	90 nts
SEQ ID NO: 139	Polypeptide encoded by SEQ ID NO: 138	30 aa
SEQ ID NO: 140	POL segment 33	90 nts
SEQ ID NO: 141	Polypeptide encoded by SEQ ID NO: 140	30 aa
SEQ ID NO: 142	POL segment 34	90 nts

	The Control of Control (Section 1) and the Control of C	1
SEQUENCE ID NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 143	Polypeptide encoded by SEQ ID NO: 142	30 aa
SEQ ID NO: 144	POL segment 35	90 nts
SEQ ID NO: 145	Polypeptide encoded by SEQ ID NO: 144	30 aa
SEQ ID NO: 146	POL segment 36	90 nts
SEQ ID NO: 147	Polypeptide encoded by SEQ ID NO: 146	30 aa
SEQ ID NO: 148	POL segment 37	90 nts
SEQ ID NO: 149	Polypeptide encoded by SEQ ID NO: 148	30 aa
SEQ ID NO: 150	POL segment 38	90 nts
SEQ ID NO: 151	Polypeptide encoded by SEQ ID NO: 150	30 aa
SEQ ID NO: 152	POL segment 39	90 nts
SEQ ID NO: 153	Polypeptide encoded by SEQ ID NO: 152	30 aa
SEQ ID NO: 154	POL segment 40	90 nts
SEQ ID NO: 155	Polypeptide encoded by SEQ ID NO: 154	30 aa
SEQ ID NO: 156	POL segment 41	90 nts
SEQ ID NO: 157	Polypeptide encoded by SEQ ID NO: 156	30 aa
SEQ ID NO: 158	POL segment 42	90 nts
SEQ ID NO: 159	Polypeptide encoded by SEQ ID NO: 158	30 aa
SEQ ID NO: 160	POL segment 43	90 nts
SEQ ID NO: 161	Polypeptide encoded by SEQ ID NO: 160	30 aa
SEQ ID NO: 162	POL segment 44	90 nts
SEQ ID NO: 163	Polypeptide encoded by SEQ ID NO: 162	30 aa
SEQ ID NO: 164	POL segment 45	90 nts
SEQ ID NO: 165	Polypeptide encoded by SEQ ID NO: 164	30 aa
SEQ ID NO: 166	POL segment 46	90 nts

SEQUENCE ID NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 167	Polypeptide encoded by SEQ ID NO: 166	30 aa
SEQ ID NO: 168	POL segment 47	90 nts
SEQ ID NO: 169	Polypeptide encoded by SEQ ID NO: 168	30 aa
SEQ ID NO: 170	POL segment 48	90 nts
SEQ ID NO: 171	Polypeptide encoded by SEQ ID NO: 170	30 aa
SEQ ID NO: 172	POL segment 49	90 nts
SEQ ID NO: 173	Polypeptide encoded by SEQ ID NO: 172	30 aa
SEQ ID NO: 174	POL segment 50	90 nts
SEQ ID NO: 175	Polypeptide encoded by SEQ ID NO: 174	30 aa
SEQ ID NO: 176	POL segment 51	90 nts
SEQ ID NO: 177	Polypeptide encoded by SEQ ID NO: 176	30 aa
SEQ ID NO: 178	POL segment 52	90 nts
SEQ ID NO: 179	Polypeptide encoded by SEQ ID NO: 178	30 aa
SEQ ID NO: 180	POL segment 53	90 nts
SEQ ID NO: 181	Polypeptide encoded by SEQ ID NO: 180	30 aa
SEQ ID NO: 182	POL segment 54	90 nts
SEQ ID NO: 183	Polypeptide encoded by SEQ ID NO: 182	30 aa
SEQ ID NO: 184	POL segment 55	90 nts
SEQ ID NO: 185	Polypeptide encoded by SEQ ID NO: 184	30 aa
SEQ ID NO: 186	POL segment 56	90 nts
SEQ ID NO: 187	Polypeptide encoded by SEQ ID NO: 186	30 aa
SEQ ID NO: 188	POL segment 57	90 nts
SEQ ID NO: 189	Polypeptide encoded by SEQ ID NO: 188	30 aa
SEQ ID NO: 190	POL segment 58	90 nts

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SEQUENCE ID	SEQUENCE	LENGTH
NUMBER		
SEQ ID NO: 191	Polypeptide encoded by SEQ ID NO: 190	30 aa
SEQ ID NO: 192	POL segment 59	90 nts
SEQ ID NO: 193	Polypeptide encoded by SEQ ID NO: 192	30 aa
SEQ ID NO: 194	POL segment 60	90 nts
SEQ ID NO: 195	Polypeptide encoded by SEQ ID NO: 194	30 aa
SEQ ID NO: 196	POL segment 61	90 nts
SEQ ID NO: 197	Polypeptide encoded by SEQ ID NO: 196	30 aa 🕠
SEQ ID NO: 198	POL segment 62	90 nts
SEQ ID NO: 199	Polypeptide encoded by SEQ ID NO: 198	30 aa
SEQ ID NO: 200	POL segment 63	90 nts
SEQ ID NO: 201	Polypeptide encoded by SEQ ID NO: 200	30 aa
SEQ ID NO: 202	POL segment 64	90 nts
SEQ ID NO: 203	Polypeptide encoded by SEQ ID NO: 202	30 aa
SEQ ID NO: 204	POL segment 65	90 nts
SEQ ID NO: 205	Polypeptide encoded by SEQ ID NO: 204	30 aa
SEQ ID NO: 206	POL segment 66	60 nts
SEQ ID NO: 207	Polypeptide encoded by SEQ ID NO: 206	20 aa
SEQ ID NO: 208	VIF segment 1	90 nts
SEQ ID NO: 209	Polypeptide encoded by SEQ ID NO: 208	30 aa
SEQ ID NO: 210	VIF segment 2	90 nts
SEQ ID NO: 211	Polypeptide encoded by SEQ ID NO: 210	30 aa
SEQ ID NO: 212	VIF segment 3	90 nts
SEQ ID NO: 213	Polypeptide encoded by SEQ ID NO: 212	30 aa
SEQ ID NO: 214	VIF segment 4	90 nts

SEQUENCE ID NUMBER	SEQUENCE .	LENGTH .
SEQ ID NO: 215	Polypeptide encoded by SEQ ID NO: 214	30 aa
SEQ ID NO: 216	VIF segment 5	90 nts
SEQ ID NO: 217	Polypeptide encoded by SEQ ID NO: 216	30 aa
SEQ ID NO: 218	VIF segment 6	90 nts
SEQ ID NO: 219	Polypeptide encoded by SEQ ID NO: 218	30 aa
SEQ ID NO: 220	VIF segment 7	90 nts
SEQ ID NO: 221	Polypeptide encoded by SEQ ID NO: 220	30 aa
SEQ ID NO: 222	VIF segment 8	90 nts
SEQ ID NO: 223	Polypeptide encoded by SEQ ID NO: 222	30 aa
SEQ ID NO: 224	VIF segment 9	90 nts
SEQ ID NO: 225	Polypeptide encoded by SEQ ID NO: 224	30 aa
SEQ ID NO: 226	VIF segment 10	90 nts
SEQ ID NO: 227	Polypeptide encoded by SEQ ID NO: 226	30 aa
SEQ ID NO: 228	VIF segment 11	90 nts
SEQ ID NO: 229	Polypeptide encoded by SEQ ID NO: 228	30 aa
SEQ ID NO: 230	VIF segment 12	81 nts
SEQ ID NO: 231	Polypeptide encoded by SEQ ID NO: 230	27 aa
SEQ ID NO: 232	VPR segment 1	90 nts
SEQ ID NO: 233	Polypeptide encoded by SEQ ID NO: 232	30 aa
SEQ ID NO: 234	VPR segment 2	90 nts
SEQ ID NO: 235	Polypeptide encoded by SEQ ID NO: 234	30 aa
SEQ ID NO: 236	VPR segment 3	90 nts
SEQ ID NO: 237	Polypeptide encoded by SEQ ID NO: 236	30 aa
SEQ ID NO: 238	VPR segment 4	90 nts

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SEQUENCE ID		
SEQUENCE ID NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 239	Polypeptide encoded by SEQ ID NO: 238	30 aa
SEQ ID NO: 240	VPR segment 5	90 nts
SEQ ID NO: 241	Polypeptide encoded by SEQ ID NO: 240	30 aa
SEQ ID NO: 242	VPR segment 6	63 nts
SEQ ID NO: 243	Polypeptide encoded by SEQ ID NO: 242	21 aa
SEQ ID NO: 244	TAT segment 1	90 nts
SEQ ID NO: 245	Polypeptide encoded by SEQ ID NO: 244	30 aa
SEQ ID NO: 246	TAT segment 2	90 nts
SEQ ID NO: 247	Polypeptide encoded by SEQ ID NO: 246	30 aa
SEQ ID NO: 248	TAT segment 3	90 nts
SEQ ID NO: 249	Polypeptide encoded by SEQ ID NO: 248	30 aa
SEQ ID NO: 250	TAT segment 4	90 nts
SEQ ID NO: 251	Polypeptide encoded by SEQ ID NO: 250	30 aa
SEQ ID NO: 252	TAT segment 5	90 nts
SEQ ID NO: 253	Polypeptide encoded by SEQ ID NO: 252	30 aa
SEQ ID NO: 254	TAT segment 6	81 nts
SEQ ID NO: 255	Polypeptide encoded by SEQ ID NO: 254	27 aa
SEQ ID NO: 256	REV segment 1	90 nts
SEQ ID NO: 257	Polypeptide encoded by SEQ ID NO: 256	30 aa
SEQ ID NO: 258	REV segment 2	90 nts
SEQ ID NO: 259	Polypeptide encoded by SEQ ID NO: 258	30 aa
SEQ ID NO: 260	REV segment 3	90 nts
SEQ ID NO: 261	Polypeptide encoded by SEQ ID NO: 260	30 aa
SEQ ID NO: 262	REV segment 4	90 nts

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SEQUENCE ID NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 263	Polypeptide encoded by SEQ ID NO: 262	30 aa
SEQ ID NO: 264	REV segment 5	90 nts
SEQ ID NO: 265	Polypeptide encoded by SEQ ID NO: 264	30 aa
SEQ ID NO: 266	REV segment 6	90 nts
SEQ ID NO: 267	Polypeptide encoded by SEQ ID NO: 266	30 aa
SEQ ID NO: 268	REV segment 7	90 nts
SEQ ID NO: 269	Polypeptide encoded by SEQ ID NO: 268	30 aa
SEQ ID NO: 270	REV segment 8	54 nts
SEQ ID NO: 271	Polypeptide encoded by SEQ ID NO: 270	18 aa
SEQ ID NO: 272	VPU segment 1	90 nts
SEQ ID NO: 273	Polypeptide encoded by SEQ ID NO: 272	30 aa
SEQ ID NO: 274	VPU segment 2	90 nts
SEQ ID NO: 275	Polypeptide encoded by SEQ ID NO: 274	30 aa
SEQ ID NO: 276	VPU segment 3	90 nts
SEQ ID NO: 277	Polypeptide encoded by SEQ ID NO: 276	30 aa
SEQ ID NO: 278	VPU segment 4	90 nts
SEQ ID NO: 279	Polypeptide encoded by SEQ ID NO: 278	30 aa
SEQ ID NO: 280	VPU segment 5	63 nts
SEQ ID NO: 281	Polypeptide encoded by SEQ ID NO: 280	21 aa
SEQ ID NO: 282	ENV segment 1	90 nts
SEQ ID NO: 283	Polypeptide encoded by SEQ ID NO: 282	30 aa
SEQ ID NO: 284	ENV segment 2	90 nts
SEQ ID NO: 285	Polypeptide encoded by SEQ ID NO: 284	30 aa
SEQ ID NO: 286	ENV segment 3	90 nts

SEQUENCE ID NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 287	Polypeptide encoded by SEQ ID NO: 286	30 aa
SEQ ID NO: 288	ENV segment 4	90 nts
SEQ ID NO: 289	Polypeptide encoded by SEQ ID NO: 288	30 aa
SEQ ID NO: 290	ENV segment 5	90 nts
SEQ ID NO: 291	Polypeptide encoded by SEQ ID NO: 290	30 aa
SEQ ID NO: 292	ENV segment 6	90 nts
SEQ ID NO: 293	Polypeptide encoded by SEQ ID NO: 292	30 aa
SEQ ID NO: 294	ENV segment 7	90 nts
SEQ ID NO: 295	Polypeptide encoded by SEQ ID NO: 294	30 aa
SEQ ID NO: 296	ENV segment 8	90 nts
SEQ ID NO: 297	Polypeptide encoded by SEQ ID NO: 296	30 aa
SEQ ID NO: 298	ENV segment 9	57 nts
SEQ ID NO: 299	Polypeptide encoded by SEQ ID NO: 298	19 aa
SEQ ID NO: 300	GAP A segment 1	90 nts
SEQ ID NO: 301	Polypeptide encoded by SEQ ID NO: 300	30 aa
SEQ ID NO: 302	GAP A segment 2	90 nts
SEQ ID NO: 303	Polypeptide encoded by SEQ ID NO: 302	30 aa
SEQ ID NO: 304	GAP A segment 3	90 nts
SEQ ID NO: 305	Polypeptide encoded by SEQ ID NO: 304	30 aa
SEQ ID NO: 306	GAP A segment 4	90 nts
SEQ ID NO: 307	Polypeptide encoded by SEQ ID NO: 306	30 aa
SEQ ID NO: 308	GAP A segment 5	90 nts
SEQ ID NO: 309	Polypeptide encoded by SEQ ID NO: 308	30 aa
SEQ ID NO: 310	GAP A segment 6	90 nts

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SEQUENCE ID NUMBER	SEQUENCE.	LENGTH
SEQ ID NO: 311	Polypeptide encoded by SEQ ID NO: 310	30 aa
SEQ ID NO: 312	GAP A segment 7	75 nts
SEQ ID NO: 313	Polypeptide encoded by SEQ ID NO: 312	25 nts
SEQ ID NO: 314	GAP B segment 1	90 nts
SEQ ID NO: 315	Polypeptide encoded by SEQ ID NO: 314	30 aa
SEQ ID NO: 316	GAP B segment 2	90 nts
SEQ ID NO: 317	Polypeptide encoded by SEQ ID NO: 316	30 aa
SEQ ID NO: 318	GAP B segment 3	90 nts
SEQ ID NO: 319	Polypeptide encoded by SEQ ID NO: 318	30 aa
SEQ ID NO: 320	GAP B segment 4	90 nts
SEQ ID NO: 321	Polypeptide encoded by SEQ ID NO: 320	30 aa
SEQ ID NO: 322	GAP B segment 5	90 nts
SEQ ID NO: 323	Polypeptide encoded by SEQ ID NO: 322	30 aa
SEQ ID NO: 324	GAP B segment 6	90 nts
SEQ ID NO: 325	Polypeptide encoded by SEQ ID NO: 324	30 aa
SEQ ID NO: 326	GAP B segment 7	90 nts
SEQ ID NO: 327	Polypeptide encoded by SEQ ID NO: 326	30 aa
SEQ ID NO: 328	GAP B segment 8	90 nts
SEQ ID NO: 329	Polypeptide encoded by SEQ ID NO: 328	30 aa
SEQ ID NO: 330	GAP B segment 9	90 nts
SEQ ID NO: 331	Polypeptide encoded by SEQ ID NO: 330	30 aa
SEQ ID NO: 332	GAP B segment 10	90 nts
SEQ ID NO: 333	Polypeptide encoded by SEQ ID NO: 332	30 aa
SEQ ID NO: 334	GAP B segment 11	90 nts

SEQUENCE ID	SEQUENCE	LENGTH
NUMBER		
SEQ ID NO: 335	Polypeptide encoded by SEQ ID NO: 334	30 aa
SEQ ID NO: 336	GAP B segment 12	90 nts .
SEQ ID NO: 337	Polypeptide encoded by SEQ ID NO: 336	30 aa
SEQ ID NO: 338	GAP B segment 13	90 nts
SEQ ID NO: 339	Polypeptide encoded by SEQ ID NO: 338	30 aa
SEQ ID NO: 340	GAP B segment 14	90 nts
SEQ ID NO: 341	Polypeptide encoded by SEQ ID NO: 340	30 aa
SEQ ID NO: 342	GAP B segment 15	90 nts
SEQ ID NO: 343	Polypeptide encoded by SEQ ID NO: 342	30 aa
SEQ ID NO: 344	GAP B segment 16	90 nts
SEQ ID NO: 345	Polypeptide encoded by SEQ ID NO: 344	30 aa
SEQ ID NO: 346	GAP B segment 17	90 nts
SEQ ID NO: 347	Polypeptide encoded by SEQ ID NO: 346	30 aa
SEQ ID NO: 348	GAP B segment 18	90 nts
SEQ ID NO: 349	Polypeptide encoded by SEQ ID NO: 348	30 aa
SEQ ID NO: 350	GAP B segment 19	90 nts
SEQ ID NO: 351	Polypeptide encoded by SEQ ID NO: 350	30 aa
SEQ ID NO: 352	GAP B segment 20	90 nts
SEQ ID NO: 353	Polypeptide encoded by SEQ ID NO: 352	30 aa
SEQ ID NO: 354	GAP B segment 21	90 nts
SEQ ID NO: 355	Polypeptide encoded by SEQ ID NO: 354	30 aa
SEQ ID NO: 356	GAP B segment 22	90 nts
SEQ ID NO: 357	Polypeptide encoded by SEQ ID NO: 356	30 aa
SEQ ID NO: 358	GAP B segment 23	90 nts

SEQUENCE ID NUMBER	SEQUENCE	<i>LENGTH</i>
SEQ ID NO: 359	Polypeptide encoded by SEQ ID NO: 358	30 aa
SEQ ID NO: 360	GAP B segment 24	90 nts
SEQ ID NO: 361	Polypeptide encoded by SEQ ID NO: 360	30 aa
SEQ ID NO: 362	GAP B segment 25	90 nts
SEQ ID NO: 363	Polypeptide encoded by SEQ ID NO: 362	30 aa
SEQ ID NO: 364	GAP B segment 26	66 nts
SEQ ID NO: 365	Polypeptide encoded by SEQ ID NO: 364	22 aa
SEQ ID NO: 366	NEF segment 1	90 nts
SEQ ID NO: 367	Polypeptide encoded by SEQ ID NO: 366	30 aa
SEQ ID NO: 368	NEF segment 2	90 nts
SEQ ID NO: 369	Polypeptide encoded by SEQ ID NO: 368	30 aa
SEQ ID NO: 370	NEF segment 3	90 nts
SEQ ID NO: 371	Polypeptide encoded by SEQ ID NO: 370	30 aa
SEQ ID NO: 372	NEF segment 4	90 nts
SEQ ID NO: 373	Polypeptide encoded by SEQ ID NO: 372	30 aa
SEQ ID NO: 374	NEF segment 5	90 nts
SEQ ID NO: 375	Polypeptide encoded by SEQ ID NO: 374	30 aa
SEQ ID NO: 376	NEF segment 6	90 nts
SEQ ID NO: 377	Polypeptide encoded by SEQ ID NO: 376	30 aa
SEQ ID NO: 378	NEF segment 7	90 nts
SEQ ID NO: 379	Polypeptide encoded by SEQ ID NO: 378	30 aa
SEQ ID NO: 380	NEF segment 8	90 nts
SEQ ID NO: 381	Polypeptide encoded by SEQ ID NO: 380	30 aa
SEQ ID NO: 382	NEF segment 9	90 nts

SEQUENCE ID NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 383	Polypeptide encoded by SEQ ID NO: 382	30 aa
SEQ ID NO: 384	NEF segment 10	90 nts
SEQ ID NO: 385	Polypeptide encoded by SEQ ID NO: 384	30 aa
SEQ ID NO: 386	NEF segment 11	90 nts
SEQ ID NO: 387	Polypeptide encoded by SEQ ID NO: 386	30 aa
SEQ ID NO: 388	NEF segment 12	90 nts
SEQ ID NO: 389	Polypeptide encoded by SEQ ID NO: 388	30 aa
SEQ ID NO: 390	NEF segment 13	78 nts
SEQ ID NO: 391	Polypeptide encoded by SEQ ID NO: 390	26 aa
SEQ ID NO: 392	HIV Cassette A1	5703 nts
SEQ ID NO: 393	Polypeptide encoded by SEQ ID NO:392	1896 aa
SEQ ID NO: 394	HIV Cassette B1	5685 nts
SEQ ID NO: 395	Polypeptide encoded by SEQ ID NO: 394	1890 aa
SEQ ID NO: 396	HIV Cassette C1	5925 nts
SEQ ID NO: 397	Polypeptide encoded by SEQ ID NO: 396	1967 aa
SEQ ID NO: 398	HIV Cassette A2	5703 nts
SEQ ID NO: 399	Polypeptide encoded by SEQ ID NO: 398	1896 aa
SEQ ID NO: 400	HIV Cassette B2	5685 nts
SEQ ID NO: 401	Polypeptide encoded by SEQ ID NO: 400	1890 aa
SEQ ID NO: 402	HIV Cassette C2	5925 nts
SEQ ID NO: 403	Polypeptide encoded by SEQ ID NO: 402	1967 aa
SEQ ID NO: 404	HIV complete Savine	17244 nts
SEQ ID NO: 405	Polypeptide encoded by SEQ ID NO: 404	5747 aa
SEQ ID NO: 406	HepC1a consensus polyprotein sequence	3011 aa

SEQUENCE ID NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 407	HepC1a segment 1	90 nts
SEQ ID NO: 408	Polypeptide encoded by SEQ ID NO: 407	30 aa
SEQ ID NO: 409	HepC1a segment 2	90 nts
SEQ ID NO: 410	Polypeptide encoded by SEQ ID NO: 409	30 aa
SEQ ID NO: 411	HepC1a segment 3	90 nts
SEQ ID NO: 412	Polypeptide encoded by SEQ ID NO: 411	30 aa
SEQ ID NO: 413	HepC1a segment 4	90 nts
SEQ ID NO: 414	Polypeptide encoded by SEQ ID NO: 413	30 aa
SEQ ID NO: 415	HepC1a segment 5	90 nts
SEQ ID NO: 416	Polypeptide encoded by SEQ ID NO: 415	30 aa
SEQ ID NO: 417	HepC1a segment 6	90 nts
SEQ ID NO: 418	Polypeptide encoded by SEQ ID NO: 417	30 aa
SEQ ID NO: 419	HepC1a segment 7	90 nts
SEQ ID NO: 420	Polypeptide encoded by SEQ ID NO: 419	30 aa
SEQ ID NO: 421	HepC1a segment 8	90 nts
SEQ ID NO: 422	Polypeptide encoded by SEQ ID NO: 421	30 aa
SEQ ID NO: 423	HepC1a segment 9	90 nts
SEQ ID NO: 424	Polypeptide encoded by SEQ ID NO: 423	30 aa
SEQ ID NO: 425	HepC1a segment 10	90 nts
SEQ ID NO: 426	Polypeptide encoded by SEQ ID NO: 425	30 aa
SEQ ID NO: 427	HepCla segment 11	90 nts
SEQ ID NO: 428	Polypeptide encoded by SEQ ID NO: 427	30 aa
SEQ ID NO: 429	HepCla segment 12	90 nts
SEQ ID NO: 430	Polypeptide encoded by SEQ ID NO: 429	30 aa

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SEQUENCE ID	GOLENCE	LENGTH
NUMBER.	SEQUENCE	LENGIH
SEQ ID NO: 431	HepC1a segment 13	90 nts
SEQ ID NO: 432	Polypeptide encoded by SEQ ID NO: 431	30 aa
SEQ ID NO: 433	HepCla segment 14	90 nts
SEQ ID NO: 434	Polypeptide encoded by SEQ ID NO: 433	30 aa
SEQ ID NO: 435	HepC1a segment 15	90 nts
SEQ ID NO: 436	Polypeptide encoded by SEQ ID NO: 435	30 aa
SEQ ID NO: 437	HepC1a segment 16	90 nts
SEQ ID NO: 438	Polypeptide encoded by SEQ ID NO: 437	30 aa
SEQ ID NO: 439	HepCla segment 17	90 nts
SEQ ID NO: 440	Polypeptide encoded by SEQ ID NO: 439	30 aa
SEQ ID NO: 441	HepC1a segment 18	90 nts
SEQ ID NO: 442	Polypeptide encoded by SEQ ID NO: 441	30 aa
SEQ ID NO: 443	HepC1a segment 19	90 nts
SEQ ID NO: 444	Polypeptide encoded by SEQ ID NO: 443	30 aa
SEQ ID NO: 445	HepC1a segment 20	90 nts
SEQ ID NO: 446	Polypeptide encoded by SEQ ID NO: 445	30 aa
SEQ ID NO: 447	HepC1a segment 21	90 nts
SEQ ID NO: 448	Polypeptide encoded by SEQ ID NO: 447	30 aa
SEQ ID NO: 449	HepC1a segment 22	90 nts
SEQ ID NO: 450	Polypeptide encoded by SEQ ID NO: 449	30 aa
SEQ ID NO: 451	HepC1a segment 23	90 nts
SEQ ID NO: 452	Polypeptide encoded by SEQ ID NO: 451	30 aa
SEQ ID NO: 453	HepC1a segment 24	90 nts
SEQ ID NO: 454	Polypeptide encoded by SEQ ID NO: 453	30 aa

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SEQUENCE ID NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 455	HepC1a segment 25	90 nts
SEQ ID NO: 456	Polypeptide encoded by SEQ ID NO: 455	30 aa
SEQ ID NO: 457	HepC1a segment 26	90 nts
SEQ ID NO: 458	Polypeptide encoded by SEQ ID NO: 457	30 aa
SEQ ID NO: 459	HepC1a segment 27	90 nts
SEQ ID NO: 460	Polypeptide encoded by SEQ ID NO: 459	30 aa
SEQ ID NO: 461	HepC1a segment 28	90 nts
SEQ ID NO: 462	Polypeptide encoded by SEQ ID NO: 461	30 aa
SEQ ID NO: 463	HepC1a segment 29	90 nts
SEQ ID NO: 464	Polypeptide encoded by SEQ ID NO: 463	30 aa
SEQ ID NO: 465	HepC1a segment 30	90 nts
SEQ ID NO: 466	Polypeptide encoded by SEQ ID NO: 465	30 aa
SEQ ID NO.: 467	HepC1a segment 31	90 nts
SEQ ID NO: 468	Polypeptide encoded by SEQ ID NO: 467	30 aa
SEQ ID NO: 469	HepC1a segment 32	90 nts
SEQ ID NO: 470	Polypeptide encoded by SEQ ID NO: 469	30 aa
SEQ ID NO: 471	HepC1a segment 33	90 nts
SEQ ID NO: 472	Polypeptide encoded by SEQ ID NO: 471	30 aa
SEQ ID NO: 473	HepC1a segment 34	90 nts
SEQ ID NO: 474	Polypeptide encoded by SEQ ID NO: 473	30 aa
SEQ ID NO: 475	HepC1a segment 35	90 nts
SEQ ID NO: 476	Polypeptide encoded by SEQ ID NO: 475	30 aa
SEQ ID NO: 477	HepC1a segment 36	90 nts
SEQ ID NO: 478	Polypeptide encoded by SEQ ID NO: 477	30 aa

SEQUENCE ID	SEQUENCE	LENGTH
NUMBER		
SEQ ID NO: 479	HepC1a segment 37	90 nts
SEQ ID NO: 480	Polypeptide encoded by SEQ ID NO: 479	30 aa
SEQ ID NO: 481	HepC1a segment 38	90 nts
SEQ ID NO: 482	Polypeptide encoded by SEQ ID NO: 481	30 aa
SEQ ID NO: 483	HepC1a segment 39	90 nts
SEQ ID NO: 484	Polypeptide encoded by SEQ ID NO: 483	30 aa
SEQ ID NO: 485	HepC1a segment 40	90 nts
SEQ ID NO: 486	Polypeptide encoded by SEQ ID NO: 485	30 aa
SEQ ID NO: 487	HepC1a segment 41	90 nts
SEQ ID NO: 488	Polypeptide encoded by SEQ ID NO: 487	30 aa
SEQ ID NO: 489	HepC1a segment 42	90 nts
SEQ ID NO: 490	Polypeptide encoded by SEQ ID NO: 489	30 aa
SEQ ID NO: 491	HepC1a segment 43	90 nts
SEQ ID NO: 492	Polypeptide encoded by SEQ ID NO: 491	30 aa
SEQ ID NO: 493	HepCla segment 44	90 nts
SEQ ID NO: 494	Polypeptide encoded by SEQ ID NO: 493	30 aa
SEQ ID NO: 495	HepCla segment 45	90 nts
SEQ ID NO: 496	Polypeptide encoded by SEQ ID NO: 495	30 aa
SEQ ID NO: 497	HepC1a segment 46	90 nts
SEQ ID NO: 498	Polypeptide encoded by SEQ ID NO: 497	30 aa
SEQ ID NO: 499	HepC1a segment 47	90 nts
SEQ ID NO: 500	Polypeptide encoded by SEQ ID NO: 499	30 aa
SEQ ID NO: 501	HepC1a segment 48	90 nts
SEQ ID NO: 502	Polypeptide encoded by SEQ ID NO: 501	30 aa

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SEQUENCE ID NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 503	HepC1a segment 49	90 nts
SEQ ID NO: 504	Polypeptide encoded by SEQ ID NO: 503	30 aa
SEQ ID NO: 505	HepC1a segment 50	90 nts
SEQ ID NO: 506	Polypeptide encoded by SEQ ID NO: 505	30 aa
SEQ ID NO: 507	HepC1a segment 51	90 nts
SEQ ID NO: 508	Polypeptide encoded by SEQ ID NO: 507	30 aa
SEQ ID NO: 509	HepC1a segment 52	90 nts
SEQ ID NO: 510	Polypeptide encoded by SEQ ID NO: 509	30 aa
SEQ ID NO: 511	HepC1a segment 53	90 nts
SEQ ID NO: 512	Polypeptide encoded by SEQ ID NO: 511	30 aa
SEQ ID NO: 513	HepC1a segment 54	90 nts
SEQ ID NO: 514	Polypeptide encoded by SEQ ID NO: 513	30 aa
SEQ ID NO: 515	HepC1a segment 55	90 nts
SEQ ID NO: 516	Polypeptide encoded by SEQ ID NO: 515	30 aa
SEQ ID NO: 517	HepC1a segment 56	90 nts
SEQ ID NO: 518	Polypeptide encoded by SEQ ID NO: 517	30 aa
SEQ ID NO: 519	HepC1a segment 57	90 nts
SEQ ID NO: 520	Polypeptide encoded by SEQ ID NO: 519	30 aa
SEQ ID NO: 521	HepC1a segment 58	90 nts
SEQ ID NO: 522	Polypeptide encoded by SEQ ID NO: 521	30 aa
SEQ ID NO: 523	HepC1a segment 59	90 nts
SEQ ID NO: 524	Polypeptide encoded by SEQ ID NO: 523	30 aa
SEQ ID NO: 525	HepC1a segment 60	90 nts
SEQ ID NO: 526	Polypeptide encoded by SEQ ID NO: 525	30 aa

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SEQUENCE ID NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 527	HepC1a segment 61	90 nts
SEQ ID NO: 528	Polypeptide encoded by SEQ ID NO: 527	30 aa
SEQ ID NO: 529	HepC1a segment 62	90 nts
SEQ ID NO: 530	Polypeptide encoded by SEQ ID NO: 529	30 aa
SEQ ID NO: 531	HepC1a segment 63	90 nts
SEQ ID NO: 532	Polypeptide encoded by SEQ ID NO: 531	30 aa
SEQ ID NO: 533	HepC1a segment 64	90 nts
SEQ ID NO: 534	Polypeptide encoded by SEQ ID NO: 533	30 aa
SEQ ID NO: 535	HepC1a segment 65	90 nts
SEQ ID NO: 536	Polypeptide encoded by SEQ ID NO: 535	30 aa
SEQ ID NO: 537	HepCla segment 66	90 nts
SEQ ID NO: 538	Polypeptide encoded by SEQ ID NO: 537	30 aa
SEQ ID NO: 539	HepCla segment 67	90 nts
SEQ ID NO: 540	Polypeptide encoded by SEQ ID NO: 539	30 aa
SEQ ID NO: 541	HepCla segment 68	90 nts
SEQ ID NO: 542	Polypeptide encoded by SEQ ID NO: 541	30 aa
SEQ ID NO: 543	HepC1a segment 69	90 nts
SEQ ID NO: 544	Polypeptide encoded by SEQ ID NO: 543	30 aa
SEQ ID NO: 545	HepC1a segment 70	90 nts
SEQ ID NO: 546	Polypeptide encoded by SEQ ID NO:545	30 aa
SEQ ID NO: 547	HepC1a segment 71	90 nts
SEQ ID NO: 548	Polypeptide encoded by SEQ ID NO: 547	30 aa
SEQ ID NO: 549	HepC1a segment 72	90 nts
SEQ ID NO: 550	Polypeptide encoded by SEQ ID NO: 549	30 aa

SEQUENCE ID NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 551	HepC1a segment 73	90 nts
SEQ ID NO: 552	Polypeptide encoded by SEQ ID NO: 551	30 aa
SEQ ID NO: 553	HepC1a segment 74	90 nts
SEQ ID NO: 554	Polypeptide encoded by SEQ ID NO: 553	30 aa
SEQ ID NO: 555	HepC1a segment 75	90 nts
SEQ ID NO: 556	Polypeptide encoded by SEQ ID NO: 555	30 aa
SEQ ID NO: 557	HepC1a segment 76	90 nts
SEQ ID NO: 558	Polypeptide encoded by SEQ ID NO: 557	30 aa
SEQ ID NO: 559	HepCla segment 77	90 nts
SEQ ID NO: 560	Polypeptide encoded by SEQ ID NO: 559	30 aa
SEQ ID NO: 561	HepC1a segment 78	90 nts
SEQ ID NO: 562	Polypeptide encoded by SEQ ID NO: 561	30 aa
SEQ ID NO: 563	HepC1a segment 79	90 nts
SEQ ID NO: 564	Polypeptide encoded by SEQ ID NO: 563	30 aa
SEQ ID NO: 565	HepC1a segment 80	90 nts
SEQ ID NO: 566	Polypeptide encoded by SEQ ID NO: 565	30 aa
SEQ ID NO: 567	HepC1a segment 81	90 nts
SEQ ID NO: 568	Polypeptide encoded by SEQ ID NO: 567	30 aa
SEQ ID NO: 569	HepC1a segment 82	90 nts
SEQ ID NO: 570	Polypeptide encoded by SEQ ID NO: 569	30 aa
SEQ ID NO: 571	HepC1a segment 83	90 nts
SEQ ID NO: 572	Polypeptide encoded by SEQ ID NO: 571	30 aa
SEQ ID NO: 573	HepC1a segment 84	90 nts
SEQ ID NO: 574	Polypeptide encoded by SEQ ID NO: 573	30 aa

SEQUENCE ID NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 575	HepC1a segment 85	90 nts
SEQ ID NO: 576	Polypeptide encoded by SEQ ID NO: 575	30 aa
SEQ ID NO: 577	HepC1a segment 86	90 nts
SEQ ID NO: 578	Polypeptide encoded by SEQ ID NO: 577	30 aa
SEQ ID NO: 579	HepC1a segment 87	90 nts
SEQ ID NO: 580	Polypeptide encoded by SEQ ID NO: 579	30 aa
SEQ ID NO: 581	HepC1a segment 88	90 nts
SEQ ID NO: 582	Polypeptide encoded by SEQ ID NO: 581	30 aa
SEQ ID NO: 583	HepCla segment 89	90 nts
SEQ ID NO: 584	Polypeptide encoded by SEQ ID NO: 583	30 aa
SEQ ID NO: 585	HepC1a segment 90	90 nts
SEQ ID NO: 586	Polypeptide encoded by SEQ ID NO: 585	30 aa
SEQ ID NO: 587	HepCla segment 91	90 nts
SEQ ID NO: 588	Polypeptide encoded by SEQ ID NO: 587	30 aa
SEQ ID NO: 589	HepC1a segment 92	90 nts
SEQ ID NO: 590	Polypeptide encoded by SEQ ID NO: 589	30 aa
SEQ ID NO: 591	HepC1a segment 93	90 nts
SEQ ID NO: 592	Polypeptide encoded by SEQ ID NO: 591	30 aa
SEQ ID NO: 593	HepC1a segment 94	90 nts
SEQ ID NO: 594	Polypeptide encoded by SEQ ID NO: 593	30 aa
SEQ ID NO: 595	HepC1a segment 95	90 nts
SEQ ID NO: 596	Polypeptide encoded by SEQ ID NO: 595	30 aa
SEQ ID NO: 597	HepC1a segment 96	90 nts
SEQ ID NO: 598	Polypeptide encoded by SEQ ID NO: 597	30 aa

SEQUENCE ID NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 599	HepC1a segment 97	90 nts
SEQ ID NO: 600	Polypeptide encoded by SEQ ID NO: 599	30 aa
SEQ ID NO: 601	HepC1a segment 98	90 nts
SEQ ID NO: 602	Polypeptide encoded by SEQ ID NO: 601	30 aa
SEQ ID NO: 603	HepC1a segment 99	90 nts
SEQ ID NO: 604	Polypeptide encoded by SEQ ID NO: 603	30 aa
SEQ ID NO: 605	HepC1a segment 100	90 nts
SEQ ID NO: 606	Polypeptide encoded by SEQ ID NO: 605	30 aa
SEQ ID NO: 607	HepCla segment 101	90 nts
SEQ ID NO: 608	Polypeptide encoded by SEQ ID NO: 607	30 aa
SEQ ID NO: 609	HepC1a segment 102	90 nts
SEQ ID NO: 610	Polypeptide encoded by SEQ ID NO: 609	30 aa
SEQ ID NO: 611	HepC1a segment 103	90 nts
SEQ ID NO: 612	Polypeptide encoded by SEQ ID NO: 611	30 aa
SEQ ID NO: 613	HepC1a segment 104	90 nts
SEQ ID NO: 614	Polypeptide encoded by SEQ ID NO: 613	30 aa
SEQ ID NO: 615	HepC1a segment 105	90 nts
SEQ ID NO: 616	Polypeptide encoded by SEQ ID NO: 615	30 aa
SEQ ID NO: 617	HepC1a segment 106	90 nts
SEQ ID NO: 618	Polypeptide encoded by SEQ ID NO: 617	30 aa
SEQ ID NO: 619	HepC1a segment 107	90 nts
SEQ ID NO: 620	Polypeptide encoded by SEQ ID NO: 619	30 aa
SEQ ID NO: 621	HepC1a segment 108	90 nts
SEQ ID NO: 622	Polypeptide encoded by SEQ ID NO: 621	30 aa

SEQUENCE ID NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 623	HepCla segment 109	90 nts
SEQ ID NO: 624	Polypeptide encoded by SEQ ID NO: 623	30 aa
SEQ ID NO: 625	HepC1a segment 110	90 nts
SEQ ID NO: 626	Polypeptide encoded by SEQ ID NO: 625	30 aa
SEQ ID NO: 627	HepCla segment 111	90 nts
SEQ ID NO: 628	Polypeptide encoded by SEQ ID NO: 627	30 aa
SEQ ID NO: 629	HepC1a segment 112	90 nts
SEQ ID NO: 630	Polypeptide encoded by SEQ ID NO: 629	30 aa
SEQ ID NO: 631	HepC1a segment 113	90 nts
SEQ ID NO: 632	Polypeptide encoded by SEQ ID NO: 631	30 aa
SEQ ID NO: 633	HepC1a segment 114	90 nts
SEQ ID NO: 634	Polypeptide encoded by SEQ ID NO: 633	30 aa
SEQ ID NO: 635	HepCla segment 115	90 nts
SEQ ID NO: 636	Polypeptide encoded by SEQ ID NO: 635	30 aa
SEQ ID NO: 637	HepC1a segment 116	90 nts
SEQ ID NO: 638	Polypeptide encoded by SEQ ID NO: 637	30 aa
SEQ ID NO: 639	HepC1a segment 117	90 nts
SEQ ID NO: 640	Polypeptide encoded by SEQ ID NO: 639	30 aa
SEQ ID NO: 641	HepC1a segment 118	90 nts
SEQ ID NO: 642	Polypeptide encoded by SEQ ID NO: 641	30 aa
SEQ ID NO: 643	HepC1a segment 119	90 nts
SEQ ID NO: 644	Polypeptide encoded by SEQ ID NO: 643	30 aa
SEQ ID NO: 645	HepC1a segment 120	90 nts
SEQ ID NO: 646	Polypeptide encoded by SEQ ID NO: 645	30 aa

SEQUENCE ID NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 647	HepC1a segment 121	90 nts
SEQ ID NO: 648	Polypeptide encoded by SEQ ID NO: 647	30 aa
SEQ ID NO: 649	HepC1a segment 122	90 nts
SEQ ID NO: 650	Polypeptide encoded by SEQ ID NO: 649	30 aa
SEQ ID NO: 651	HepC1a segment 123	90 nts
SEQ ID NO: 652	Polypeptide encoded by SEQ ID NO: 651	30 aa
SEQ ID NO: 653	HepC1a segment 124	90 nts
SEQ ID NO: 654	Polypeptide encoded by SEQ ID NO: 653	30 aa
SEQ ID NO: 655	HepC1a segment 125	90 nts
SEQ ID NO: 656	Polypeptide encoded by SEQ ID NO: 655	30 aa
SEQ ID NO: 657	HepC1a segment 126	90 nts
SEQ ID NO: 658	Polypeptide encoded by SEQ ID NO: 657	30 aa
SEQ ID NO: 659	HepC1a segment 127	90 nts
SEQ ID NO: 660	Polypeptide encoded by SEQ ID NO: 659	30 aa
SEQ ID NO: 661	HepC1a segment 128	90 nts
SEQ ID NO: 662	Polypeptide encoded by SEQ ID NO: 661	30 aa
SEQ ID NO: 663	HepC1a segment 129	90 nts
SEQ ID NO: 664	Polypeptide encoded by SEQ ID NO: 663	30 aa
SEQ ID NO: 665	HepC1a segment 130	90 nts
SEQ ID NO: 666	Polypeptide encoded by SEQ ID NO: 665	30 aa
SEQ ID NO: 667	HepC1a segment 131	90 nts
SEQ ID NO: 668	Polypeptide encoded by SEQ ID NO: 667	30 aa
SEQ ID NO: 669	HepC1a segment 132	90 nts
SEQ ID NO: 670	Polypeptide encoded by SEQ ID NO: 669	30 aa

SEQUENCE ID	SEQUENCE	LENGTH
NUMBER		
SEQ ID NO: 671	HepC1a segment 133	90 nts
SEQ ID NO: 672	Polypeptide encoded by SEQ ID NO: 671	30 aa
SEQ ID NO: 673	HepC1a segment 134	90 nts
SEQ ID NO: 674	Polypeptide encoded by SEQ ID NO: 673	30 aa
SEQ ID NO: 675	HepC1a segment 135	90 nts
SEQ ID NO: 676	Polypeptide encoded by SEQ ID NO: 675	30 aa
SEQ ID NO: 677	HepC1a segment 136	90 nts
SEQ ID NO: 678	Polypeptide encoded by SEQ ID NO: 677	30 aa
SEQ ID NO: 679	HepC1a segment 137	90 nts
SEQ ID NO: 680	Polypeptide encoded by SEQ ID NO: 679	30 aa
SEQ ID NO: 681	HepC1a segment 138	90 nts
SEQ ID NO: 682	Polypeptide encoded by SEQ ID NO: 681	30 aa
SEQ ID NO: 683	HepCla segment 139	90 nts
SEQ ID NO: 684	Polypeptide encoded by SEQ ID NO: 683	30 aa
SEQ ID NO: 685	HepC1a segment 140	90 nts
SEQ ID NO: 686	Polypeptide encoded by SEQ ID NO: 685	30 aa
SEQ ID NO: 687	HepCla segment 141	90 nts
SEQ ID NO: 688	Polypeptide encoded by SEQ ID NO: 687	30 aa
SEQ ID NO: 689	HepCla segment 142	90 nts
SEQ ID NO: 690	Polypeptide encoded by SEQ ID NO: 689	30 aa
SEQ ID NO: 691	HepCla segment 143	90 nts
SEQ ID NO: 692	Polypeptide encoded by SEQ ID NO: 691	30 aa
SEQ ID NO: 693	HepCla segment 144	90 nts
SEQ ID NO: 694	Polypeptide encoded by SEQ ID NO: 693	30 aa

SEQUENCE ID NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 695	HepC1a segment 145	90 nts
SEQ ID NO: 696	Polypeptide encoded by SEQ ID NO: 695	30 aa
SEQ ID NO: 697	HepC1a segment 146	90 nts
SEQ ID NO: 698	Polypeptide encoded by SEQ ID NO: 697	30 aa
SEQ ID NO: 699	HepC1a segment 147	90 nts
SEQ ID NO: 700	Polypeptide encoded by SEQ ID NO: 699	30 aa
SEQ ID NO: 701	HepC1a segment 148	90 nts
SEQ ID NO: 702	Polypeptide encoded by SEQ ID NO: 701	30 aa
SEQ ID NO: 703	HepC1a segment 149	90 nts .
SEQ ID NO: 704	Polypeptide encoded by SEQ ID NO: 703	30 aa
SEQ ID NO: 705	HepC1a segment 150	90 nts
SEQ ID NO: 706	Polypeptide encoded by SEQ ID NO: 705	30 aa
SEQ ID NO: 707	HepC1a segment 151	90 nts
SEQ ID NO: 708	Polypeptide encoded by SEQ ID NO: 707	30 aa
SEQ ID NO: 709	HepC1a segment 152	90 nts
SEQ ID NO: 710	Polypeptide encoded by SEQ ID NO: 709	30 aa
SEQ ID NO: 711	HepC1a segment 153	90 nts
SEQ ID NO: 712	Polypeptide encoded by SEQ ID NO: 711	30 aa
SEQ ID NO: 713	HepCla segment 154	90 nts
SEQ ID NO: 714	Polypeptide encoded by SEQ ID NO: 713	30 aa
SEQ ID NO: 715	HepC1a segment 155	90 nts
SEQ ID NO: 716	Polypeptide encoded by SEQ ID NO: 715	30 aa
SEQ ID NO: 717	HepC1a segment 156	90 nts
SEQ ID NO: 718	Polypeptide encoded by SEQ ID NO: 717	30 aa

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SEQUENCE ID	SEQUENCE	LENGTH
NUMBER	BEQUENCE	
SEQ ID NO: 719	HepC1a segment 157	90 nts
SEQ ID NO: 720	Polypeptide encoded by SEQ ID NO: 719	30 aa
SEQ ID NO: 721	HepC1a segment 158	90 nts
SEQ ID NO: 722	Polypeptide encoded by SEQ ID NO: 721	30 aa
SEQ ID NO: 723	HepC1a segment 159	90 nts
SEQ ID NO: 724	Polypeptide encoded by SEQ ID NO: 723	30 aa
SEQ ID NO: 725	HepC1a segment 160	90 nts
SEQ ID NO: 726	Polypeptide encoded by SEQ ID NO: 725	30 aa
SEQ ID NO: 727	HepC1a segment 161	90 nts
SEQ ID NO: 728	Polypeptide encoded by SEQ ID NO: 727	30 aa
SEQ ID NO: 729	HepC1a segment 162	90 nts
SEQ ID NO: 730	Polypeptide encoded by SEQ ID NO: 729	30 aa
SEQ ID NO: 731	HepCla segment 163	90 nts
SEQ ID NO: 732	Polypeptide encoded by SEQ ID NO: 731	30 aa
SEQ ID NO: 733	HepCla segment 164	90 nts
SEQ ID NO: 734	Polypeptide encoded by SEQ ID NO: 733	30 aa
SEQ ID NO: 735	HepC1a segment 165	90 nts
SEQ ID NO: 736	Polypeptide encoded by SEQ ID NO: 735	30 aa
SEQ ID NO: 737	HepC1a segment 166	90 nts
SEQ ID NO: 738	Polypeptide encoded by SEQ ID NO: 737	30 aa
SEQ ID NO: 739	HepC1a segment 167	90 nts
SEQ ID NO: 740	Polypeptide encoded by SEQ ID NO: 739	30 aa
SEQ ID NO: 741	HepC1a segment 168	90 nts
SEQ ID NO: 742	Polypeptide encoded by SEQ ID NO: 741	30 aa

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SEQUENCE ID NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 743	HepC1a segment 169	90 nts
SEQ ID NO: 744	Polypeptide encoded by SEQ ID NO: 743	30 aa
SEQ ID NO: 745	HepC1a segment 170	90 nts
SEQ ID NO: 746	Polypeptide encoded by SEQ ID NO: 745	30 aa
SEQ ID NO: 747	HepC1a segment 171	90 nts
SEQ ID NO: 748	Polypeptide encoded by SEQ ID NO: 747	30 aa
SEQ ID NO: 749	HepC1a segment 172	90 nts
SEQ ID NO: 750	Polypeptide encoded by SEQ ID NO: 749	30 aa
SEQ ID NO: 751	HepC1a segment 173	90 nts
SEQ ID NO: 752	Polypeptide encoded by SEQ ID NO: 751	30 aa
SEQ ID NO: 753	HepC1a segment 174	90 nts
SEQ ID NO: 754	Polypeptide encoded by SEQ ID NO: 753	30 aa
SEQ ID NO: 755	HepC1a segment 175	90 nts
SEQ ID NO: 756	Polypeptide encoded by SEQ ID NO: 755	30 aa
SEQ ID NO: 757	HepC1a segment 176	90 nts
SEQ ID NO: 758	Polypeptide encoded by SEQ ID NO: 757	30 aa
SEQ ID NO: 759	HepC1a segment 177	90 nts
SEQ ID NO: 760	Polypeptide encoded by SEQ ID NO: 759	30 aa
SEQ ID NO: 761	HepC1a segment 178	90 nts
SEQ ID NO: 762	Polypeptide encoded by SEQ ID NO: 761	30 aa
SEQ ID NO: 763	HepC1a segment 179	90 nts
SEQ ID NO: 764	Polypeptide encoded by SEQ ID NO: 763	30 aa
SEQ ID NO: 765	HepC1a segment 180	90 nts
SEQ ID NO: 766	Polypeptide encoded by SEQ ID NO: 765	30 aa

SEQUENCE ID	SEQUENCE	LENGTH
NUMBER		
SEQ ID NO: 767	HepCla segment 181	90 nts
SEQ ID NO: 768	Polypeptide encoded by SEQ ID NO: 767	30 aa
SEQ ID NO: 769	HepC1a segment 182	90 nts
SEQ ID NO: 770	Polypeptide encoded by SEQ ID NO: 769	30 aa
SEQ ID NO: 771	HepC1a segment 183	90 nts
SEQ ID NO: 772	Polypeptide encoded by SEQ ID NO: 771	·30 aa
SEQ ID NO: 773	HepC1a segment 184	90 nts
SEQ ID NO: 774	Polypeptide encoded by SEQ ID NO: 773	30 aa
SEQ ID NO: 775	HepC1a segment 185	90 nts
SEQ ID NO: 776	Polypeptide encoded by SEQ ID NO: 775	30 aa
SEQ ID NO: 777	HepC1a segment 186	90 nts
SEQ ID NO: 778	Polypeptide encoded by SEQ ID NO: 777	30 aa
SEQ ID NO: 779	HepC1a segment 187	90 nts
SEQ ID NO: 780	Polypeptide encoded by SEQ ID NO: 779	30 aa
SEQ ID NO: 781	HepC1a segment 188	90 nts
SEQ ID NO: 782	Polypeptide encoded by SEQ ID NO: 781	30 aa
SEQ ID NO: 783	HepC1a segment 189	90 nts
SEQ ID NO: 784	Polypeptide encoded by SEQ ID NO: 783	30 aa
SEQ ID NO: 785	HepC1a segment 190	90 nts
SEQ ID NO: 786	Polypeptide encoded by SEQ ID NO: 785	30 aa
SEQ ID NO: 787	HepC1a segment 191	90 nts
SEQ ID NO: 788	Polypeptide encoded by SEQ ID NO: 787	30 aa
SEQ ID NO: 789	HepC1a segment 192	90 nts
SEQ ID NO: 790	Polypeptide encoded by SEQ ID NO: 789	30 aa

SEQUENCE ID NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 791	HepC1a segment 193	90 nts
SEQ ID NO: 792	Polypeptide encoded by SEQ ID NO: 791	30 aa
SEQ ID NO: 793	HepC1a segment 194	90 nts
SEQ ID NO: 794	Polypeptide encoded by SEQ ID NO: 793	30 aa
SEQ ID NO: 795	HepC1a segment 195	90 nts
SEQ ID NO: 796	Polypeptide encoded by SEQ ID NO: 795	30 aa
SEQ ID NO: 797	HepC1a segment 196	90 nts
SEQ ID NO: 798	Polypeptide encoded by SEQ ID NO: 797	30 aa
SEQ ID NO: 799	HepC1a segment 197	90 nts
SEQ ID NO: 800	Polypeptide encoded by SEQ ID NO: 799	30 aa
SEQ ID NO: 801	HepC1a segment 198	90 nts
SEQ ID NO: 802	Polypeptide encoded by SEQ ID NO: 801	30 aa
SEQ ID NO: 803	HepC1a segment 199	90 nts
SEQ ID NO: 804	Polypeptide encoded by SEQ ID NO: 803	30 aa
SEQ ID NO: 805	HepC1a segment 200	90 nts
SEQ ID NO: 806	Polypeptide encoded by SEQ ID NO: 805	30 aa
SEQ ID NO: 807	HepC1a segment 201	45 nts
SEQ ID NO: 808	Polypeptide encoded by SEQ ID NO: 807	15 aa
SEQ ID NO: 809	HepC1a scrambled	17955 nts
SEQ ID NO: 810	Polypeptide encoded by SEQ ID NO: 809	5985 aa
SEQ ID NO: 811	HepC Cassette A	6065 nts
SEQ ID NO: 812	Polypeptide encoded by SEQ ID NO: 811	2011 aa
SEQ ID NO: 813	HepC Cassette B	6069 nts
SEQ ID NO: 814	Polypeptide encoded by SEQ ID NO: 813	2010 aa

SEQUENCE ID NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 815	HepC Cassette C	6030 nts
SEQ ID NO: 816	Polypeptide encoded by SEQ ID NO: 815	1997 aa
SEQ ID NO: 817	gp100 consensus polypeptide	661 aa
SEQ ID NO: 818	MART consensus polypeptide	118 aa
SEQ ID NO: 819	TRP-1 consensus polypeptide	248 aa
SEQ ID NO: 820	Tyros consensus polypeptide	529 aa
SEQ ID NO: 821	TRP2 consensus polypeptide	519 aa
SEQ ID NO: 822	MC1R consensus polypeptide	317 aa
SEQ ID NO: 823	MUC1F consensus polypeptide	125 aa
SEQ ID NO: 824	MUC1R consensus polypeptide	312 aa
SEQ ID NO: 825	BAGE consensus polypeptide	43 aa
SEQ ID NO: 826	GAGE-1 consensus polypeptide	138 aa
SEQ ID NO: 827	gp100ln4 consensus polypeptide	51 aa
SEQ ID NO: 828	MAGE-1 consensus polypeptide	309 aa
SEQ ID NO: 829	MAGE-3 consensus polypeptide	314 aa
SEQ ID NO: 830	PRAME consensus polypeptide	509 aa
SEQ ID NO: 831	TRP2IN2 consensus polypeptide	54 aa
SEQ ID NO: 832	NYNSO1a consensus polypeptide	180 aa
SEQ ID NO: 833	NYNSO1b consensus polypeptide	58 aa
SEQ ID NO: 834	LAGE1 consensus polypeptide	180 aa
SEQ ID NO: 835	gp100 segment 1	90 nts
SEQ ID NO: 836	Polypeptide encoded by SEQ ID NO: 835	30 aa
SEQ ID NO: 837	gp100 segment 2	90 nts
SEQ ID NO: 838	Polypeptide encoded by SEQ ID NO: 837	30 aa

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SEQUENCE ID NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 839	gp100 segment 3	90 nts
SEQ ID NO: 840	Polypeptide encoded by SEQ ID NO: 839	30 aa
SEQ ID NO: 841	gp100 segment 4	90 nts
SEQ ID NO: 842	Polypeptide encoded by SEQ ID NO: 841	30 aa
SEQ ID NO: 843	gp100 segment 5	90 nts
SEQ ID NO: 844	Polypeptide encoded by SEQ ID NO: 843	30 aa
SEQ ID NO: 845	gp100 segment 6	90 nts
SEQ ID NO: 846	Polypeptide encoded by SEQ ID NO: 845	30 aa
SEQ ID NO: 847	gp100 segment 7	90 nts
SEQ ID NO: 848	Polypeptide encoded by SEQ ID NO: 847	30 aa
SEQ ID NO: 849	gp100 segment 8	90 nts
SEQ ID NO: 850	Polypeptide encoded by SEQ ID NO: 849	30 aa
SEQ ID NO: 851	gp100 segment 9	90 nts
SEQ ID NO: 852	Polypeptide encoded by SEQ ID NO: 851	30 aa
SEQ ID NO: 853	gp100 segment 10	90 nts
SEQ ID NO: 854	Polypeptide encoded by SEQ ID NO: 853	30 aa
SEQ ID NO: 855	gp100 segment 11	90 nts
SEQ ID NO: 856	Polypeptide encoded by SEQ ID NO: 855	30 aa
SEQ ID NO: 857	gp100 segment 12	90 nts
SEQ ID NO: 858	Polypeptide encoded by SEQ ID NO: 857	30 aa
SEQ ID NO: 859	gp100 segment 13	90 nts
SEQ ID NO: 860	Polypeptide encoded by SEQ ID NO: 859	30 aa
SEQ ID NO: 861	gp100 segment 14	90 nts
SEQ ID NO: 862	Polypeptide encoded by SEQ ID NO: 861	30 aa

SEQUENCE ID	SEQUENCE	LENGTH
NUMBER		
SEQ ID NO: 863	gp100 segment 15	90 nts
SEQ ID NO: 864	Polypeptide encoded by SEQ ID NO: 863	30 aa
SEQ ID NO: 865	gp100 segment 16	90 nts
SEQ ID NO: 866	Polypeptide encoded by SEQ ID NO: 865	30 aa
SEQ ID NO: 867	gp100 segment 17	90 nts
SEQ ID NO: 868	Polypeptide encoded by SEQ ID NO: 867	30 aa
SEQ ID NO: 869	gp100 segment 18	90 nts
SEQ ID NO: 870	Polypeptide encoded by SEQ ID NO: 869	30 aa
SEQ ID NO: 871	gp100 segment 19	90 nts
SEQ ID NO: 872	Polypeptide encoded by SEQ ID NO: 871	30 aa
SEQ ID NO: 873	gp100 segment 20	90 nts
SEQ ID NO: 874	Polypeptide encoded by SEQ ID NO: 873	30 aa
SEQ ID NO: 875	gp100 segment 21	90 nts
SEQ ID NO: 876	Polypeptide encoded by SEQ ID NO: 875	30 aa
SEQ ID NO: 877	gp100 segment 22	90 nts
SEQ ID NO: 878	Polypeptide encoded by SEQ ID NO: 877	30 aa
SEQ ID NO: 879	gp100 segment 23	90 nts
SEQ ID NO: 880	Polypeptide encoded by SEQ ID NO: 879	30 aa
SEQ ID NO: 881	gp100 segment 24	90 nts
SEQ ID NO: 882	Polypeptide encoded by SEQ ID NO: 881	30 aa
SEQ ID NO: 883	gp100 segment 25	90 nts
SEQ ID NO: 884	Polypeptide encoded by SEQ ID NO: 883	30 aa
SEQ ID NO: 885	gp100 segment 26	90 nts
SEQ ID NO: 886	Polypeptide encoded by SEQ ID NO: 885	30 aa

SEQUENCE ID	SEQUENCE	LENGTH
NUMBER		
SEQ ID NO: 887	gp100 segment 27	90 nts
SEQ ID NO: 888	Polypeptide encoded by SEQ ID NO: 887	30 aa
SEQ ID NO: 889	gp100 segment 28	90 nts
SEQ ID NO: 890	Polypeptide encoded by SEQ ID NO: 889	30 aa
SEQ ID NO: 891	gp100 segment 29	90 nts
SEQ ID NO: 892	Polypeptide encoded by SEQ ID NO: 891	30 aa
SEQ ID NO: 893	gp100 segment 30	90 nts
SEQ ID NO: 894	Polypeptide encoded by SEQ ID NO: 893	30 aa
SEQ ID NO: 895	gp100 segment 31	90 nts
SEQ ID NO: 896	Polypeptide encoded by SEQ ID NO: 895	30 aa
SEQ ID NO: 897	gp100 segment 32	90 nts
SEQ ID NO: 898	Polypeptide encoded by SEQ ID NO: 897	30 aa
SEQ ID NO: 899	gp100 segment 33	90 nts
SEQ ID NO: 900	Polypeptide encoded by SEQ ID NO: 899	30 aa
SEQ ID NO: 901	gp100 segment 34	90 nts
SEQ ID NO: 902	Polypeptide encoded by SEQ ID NO: 901	30 aa
SEQ ID NO: 903	gp100 segment 35	90 nts
SEQ ID NO: 904	Polypeptide encoded by SEQ ID NO: 903	30 aa
SEQ ID NO: 905	gp100 segment 36	90 nts
SEQ ID NO: 906	Polypeptide encoded by SEQ ID NO: 905	30 aa
SEQ ID NO: 907	gp100 segment 37	90 nts
SEQ ID NO: 908	Polypeptide encoded by SEQ ID NO: 907	30 aa
SEQ ID NO: 909	gp100 segment 38	90 nts
SEQ ID NO: 910	Polypeptide encoded by SEQ ID NO: 909	30 aa

SEQUENCE ID	SEQUENCE	LENGTH
NUMBER		
SEQ ID NO: 911	gp100 segment 39	90 nts
SEQ ID NO: 912	Polypeptide encoded by SEQ ID NO: 911	30 aa
SEQ ID NO: 913	gp100 segment 40	90 nts
SEQ ID NO: 914	Polypeptide encoded by SEQ ID NO: 913	30 aa
SEQ ID NO: 915	gp100 segment 41	90 nts
SEQ ID NO: 916	Polypeptide encoded by SEQ ID NO: 915	30 aa
SEQ ID NO: 917	gp100 segment 42	90 nts
SEQ ID NO: 918	Polypeptide encoded by SEQ ID NO: 917	30 aa
SEQ ID NO: 919	gp100 segment 43	90 nts
SEQ ID NO: 920	Polypeptide encoded by SEQ ID NO: 919	30 aa
SEQ ID NO: 921	gp100 segment 44	60nts
SEQ ID NO: 922	Polypeptide encoded by SEQ ID NO: 921	20 aa
SEQ ID NO: 923	MART segment 1	90 nts
SEQ ID NO: 924	Polypeptide encoded by SEQ ID NO: 923	30 aa
SEQ ID NO: 925	.MART segment 2	90 nts
SEQ ID NO: 926	Polypeptide encoded by SEQ ID NO: 925	30 aa
SEQ ID NO: 927	MART segment 3	90 nts
SEQ ID NO: 928	Polypeptide encoded by SEQ ID NO: 927	30 aa
SEQ ID NO: 929	MART segment 4	90 nts
SEQ ID NO: 930	Polypeptide encoded by SEQ ID NO: 929	30 aa
SEQ ID NO: 931	MART segment 5	90 nts
SEQ ID NO: 932	Polypeptide encoded by SEQ ID NO: 931	30 aa
SEQ ID NO: 933	MART segment 6	90 nts
ȘEQ ID NO: 934	Polypeptide encoded by SEQ ID NO: 933	30 aa

SEQUENCE ID NUMBER	SEQUENCE	LENGTH
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SEQ ID NO: 935	MART segment 7	90 nts
SEQ ID NO: 936	Polypeptide encoded by SEQ ID NO: 935	30 aa
SEQ ID NO: 937	MART segment 8	51 nts
SEQ ID NO: 938	Polypeptide encoded by SEQ ID NO: 937	17 aa
SEQ ID NO: 939	trp-1 segment 1	90 nts
SEQ ID NO: 940	Polypeptide encoded by SEQ ID NO: 939	30 aa
SEQ ID NO: 941	trp-1 segment 2	90 nts
SEQ ID NO: 942	Polypeptide encoded by SEQ ID NO: 941	30 aa
SEQ ID NO: 943	trp-1 segment 3	90 nts
SEQ ID NO: 944	Polypeptide encoded by SEQ ID NO: 943	30 aa
SEQ ID NO: 945	trp-1 segment 4	90 nts
SEQ ID NO: 946	Polypeptide encoded by SEQ ID NO: 945	30 aa
SEQ ID NO: 947	trp-1 segment 5	90 nts
SEQ ID NO: 948	Polypeptide encoded by SEQ ID NO: 947	30 aa
SEQ ID NO: 949	trp-1 segment 6	90 nts
SEQ ID NO: 950	Polypeptide encoded by SEQ ID NO: 949	30 aa
SEQ ID NO: 951	trp-1 segment 7	90 nts
SEQ ID NO: 952	Polypeptide encoded by SEQ ID NO: 951	30 aa
SEQ ID NO: 953	trp-1 segment 8	90 nts
SEQ ID NO: 954	Polypeptide encoded by SEQ ID NO: 953	30 aa
SEQ ID NO: 955	trp-1 segment 9	90 nts
SEQ ID NO: 956	Polypeptide encoded by SEQ ID NO: 955	30 aa
SEQ ID NO: 957	trp-1 segment 10	90 nts
SEQ ID NO: 958	Polypeptide encoded by SEQ ID NO: 957	30 aa

SEQUENCE ID NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 959	trp-1 segment 11	90 nts
SEQ ID NO: 960	Polypeptide encoded by SEQ ID NO: 959	30 aa
SEQ ID NO: 961	trp-1 segment 12	90 nts
SEQ ID NO: 962	Polypeptide encoded by SEQ ID NO: 961	30 aa
SEQ ID NO: 963	trp-1 segment 13	90 nts
SEQ ID NO: 964	Polypeptide encoded by SEQ ID NO: 963	30 aa
SEQ ID NO: 965	trp-1 segment 14	90 nts
SEQ ID NO: 966	Polypeptide encoded by SEQ ID NO: 965	30 aa
SEQ ID NO: 967	trp-1 segment 15	90 nts
SEQ ID NO: 968	Polypeptide encoded by SEQ ID NO: 967	30 aa
SEQ ID NO: 969	trp-1 segment 16	81 nts
SEQ ID NO: 970	Polypeptide encoded by SEQ ID NO: 969	27 aa
SEQ ID NO: 971	tyros segment 1	90 nts
SEQ ID NO: 972	Polypeptide encoded by SEQ ID NO: 971	30 aa
SEQ ID NO: 973	tyros segment 2	90 nts
SEQ ID NO: 974	Polypeptide encoded by SEQ ID NO: 973	30 aa
SEQ ID NO: 975	tyros segment 3	90 nts
SEQ ID NO: 976	Polypeptide encoded by SEQ ID NO: 975	30 aa
SEQ ID NO: 977	tyros segment 4	90 nts
SEQ ID NO: 978	Polypeptide encoded by SEQ ID NO: 977	30 aa
SEQ ID NO: 979	tyros segment 5	90 nts
SEQ ID NO: 980	Polypeptide encoded by SEQ ID NO: 979	30 aa
SEQ ID NO: 981	tyros segment 6	90 nts
SEQ ID NO: 982	Polypeptide encoded by SEQ ID NO: 981	30 aa

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SEQUENCE ID NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 983	tyros segment 7	90 nts
SEQ ID NO: 984	Polypeptide encoded by SEQ ID NO: 983	30 aa
SEQ ID NO: 985	tyros segment 8	90 nts
SEQ ID NO: 986	Polypeptide encoded by SEQ ID NO: 985	30 aa
SEQ ID NO: 987	tyros segment 9	90 nts
SEQ ID NO: 988	Polypeptide encoded by SEQ ID NO: 987	30 aa
SEQ ID NO: 989	tyros segment 10	90 nts
SEQ ID NO: 990	Polypeptide encoded by SEQ ID NO: 989	30 aa
SEQ ID NO: 991	tyros segment 11	90 nts
SEQ ID NO: 992	Polypeptide encoded by SEQ ID NO: 991	30 aa
SEQ ID NO: 993	tyros segment 12	90 nts
SEQ ID NO: 994	Polypeptide encoded by SEQ ID NO: 993	30 aa
SEQ ID NO: 995	tyros segment 13	90 nts
SEQ ID NO: 996	Polypeptide encoded by SEQ ID NO: 995	30 aa
SEQ ID NO: 997	tyros segment 14	90 nts
SEQ ID NO: 998	Polypeptide encoded by SEQ ID NO: 997	30 aa
SEQ ID NO: 999	tyros segment 15	90 nts
SEQ ID NO: 1000	Polypeptide encoded by SEQ ID NO: 999	30 aa
SEQ ID NO: 1001	tyros segment 16	90 nts
SEQ ID NO: 1002	Polypeptide encoded by SEQ ID NO: 1001	30 aa
SEQ ID NO: 1003	tyros segment 17	90 nts
SEQ ID NO: 1004	Polypeptide encoded by SEQ ID NO: 1003	30 aa
SEQ ID NO: 1005	tyros segment 18	90 nts
SEQ ID NO: 1006	Polypeptide encoded by SEQ ID NO: 1005	30 aa

表表。\$P\$ 20 · 20 · 10 · 10 · 10 · 10 · 10 · 10 ·	· 表示: - 表示: - 表示: - 表示 表示 - 表示 - 表示 - 表示	A STATE PROGRAM A GARAGE
SEQUENCE ID NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 1007	tyros segment 19	90 nts
SEQ ID NO: 1008	Polypeptide encoded by SEQ ID NO: 1007	30 aa
SEQ ID NO: 1009	tyros segment 20	90 nts
SEQ ID NO: 1010	Polypeptide encoded by SEQ ID NO: 1009	30 aa
SEQ ID NO: 1011	tyros segment 21	90 nts
SEQ ID NO: 1012	Polypeptide encoded by SEQ ID NO: 1011	30 aa
SEQ ID NO: 1013	tyros segment 22	90 nts
SEQ ID NO: 1014	Polypeptide encoded by SEQ ID NO: 1013	30 aa
SEQ ID NO: 1015	tyros segment 23	90 nts
SEQ ID NO: 1016	Polypeptide encoded by SEQ ID NO: 1015	30 aa
SEQ ID NO: 1017	tyros segment 24	90 nts
SEQ ID NO: 1018	Polypeptide encoded by SEQ ID NO: 1017	30 aa
SEQ ID NO: 1019	tyros segment 25	90 nts
SEQ ID NO: 1020	Polypeptide encoded by SEQ ID NO: 1019	30 aa
SEQ ID NO: 1021	tyros segment 26	90 nts
SEQ ID NO: 1022	Polypeptide encoded by SEQ ID NO: 1021	30 aa
SEQ ID NO: 1023	tyros segment 27	90 nts
SEQ ID NO: 1024	Polypeptide encoded by SEQ ID NO: 1023	30 aa
SEQ ID NO: 1025	tyros segment 28	90 nts
SEQ ID NO: 1026	Polypeptide encoded by SEQ ID NO: 1025	30 aa
SEQ ID NO: 1027	tyros segment 29	90 nts
SEQ ID NO: 1028	Polypeptide encoded by SEQ ID NO: 1027	30 aa
SEQ ID NO: 1029	tyros segment 30	90 nts
SEQ ID NO: 1030	Polypeptide encoded by SEQ ID NO: 1029	30 aa

SEQUENCE ID	SEQUENCE	LENGTH
NUMBER		
SEQ ID NO: 1031	tyros segment 31	90 nts
SEQ ID NO: 1032	Polypeptide encoded by SEQ ID NO: 1031	30 aa
SEQ ID NO: 1033	tyros segment 32	90 nts
SEQ ID NO: 1034	Polypeptide encoded by SEQ ID NO: 1033	30 aa
SEQ ID NO: 1035	tyros segment 33	90 nts
SEQ ID NO: 1036	Polypeptide encoded by SEQ ID NO: 1035	30 aa
SEQ ID NO: 1037	tyros segment 34	90 nts
SEQ ID NO: 1038	Polypeptide encoded by SEQ ID NO: 1037	30 aa
SEQ ID NO: 1039	tyros segment 35	69 nts
SEQ ID NO: 1040	Polypeptide encoded by SEQ ID NO: 1039	23 aa
SEQ ID NO: 1041	trp2 segment 1	90 nts
SEQ ID NO: 1042	Polypeptide encoded by SEQ ID NO: 1041	30 aa
SEQ ID NO: 1043.	trp2 segment 2	90 nts
SEQ ID NO: 1044	Polypeptide encoded by SEQ ID NO: 1043	30 aa
SEQ ID NO: 1045	trp2 segment 3	90 nts
SEQ ID NO: 1046	Polypeptide encoded by SEQ ID NO: 1045	30 aa
SEQ ID NO: 1047	trp2 segment 4	90 nts
SEQ ID NO: 1048	Polypeptide encoded by SEQ ID NO: 1047	30 aa
SEQ ID NO: 1049	trp2 segment 5	90 nts
SEQ ID NO: 1050	Polypeptide encoded by SEQ ID NO: 1049	30 aa
SEQ ID NO: 1051	trp2 segment 6	90 nts
SEQ ID NO: 1052	Polypeptide encoded by SEQ ID NO: 1051	30 aa
SEQ ID NO: 1053	trp2 segment 7	90 nts
SEQ ID NO: 1054	Polypeptide encoded by SEQ ID NO: 1053	30 aa

SEQUENCE ID	SEQUENCE	<i>LENGTH</i>
NUMBER		
SEQ ID NO: 1055	trp2 segment 8	90 nts
SEQ ID NO: 1056	Polypeptide encoded by SEQ ID NO: 1055	30 aa
SEQ ID NO: 1057	trp2 segment 9	90 nts
SEQ ID NO: 1058	Polypeptide encoded by SEQ ID NO: 1057	30 aa
SEQ ID NO: 1059	trp2 segment 10	90 nts
SEQ ID NO: 1060	Polypeptide encoded by SEQ ID NO: 1059	30 aa
SEQ ID NO: 1061	trp2 segment 11	90 nts
SEQ ID NO: 1062	Polypeptide encoded by SEQ ID NO: 1061	30 aa
SEQ ID NO: 1063	trp2 segment 12	90 nts
SEQ ID NO: 1064	Polypeptide encoded by SEQ ID NO: 1063	30 aa
SEQ ID NO: 1065	trp2 segment 13	90 nts
SEQ ID NO: 1066	Polypeptide encoded by SEQ ID NO: 1065	30 aa
SEQ ID NO: 1067	trp2 segment 14	90 nts
SEQ ID NO: 1068	Polypeptide encoded by SEQ ID NO: 1067	30 aa
SEQ ID NO: 1069	trp2 segment 15	90 nts
SEQ ID NO: 1070	Polypeptide encoded by SEQ ID NO: 1069	30 aa
SEQ ID NO: 1071	trp2 segment 16	90 nts
SEQ ID NO: 1072	Polypeptide encoded by SEQ ID NO: 1071	30 aa
SEQ ID NO: 1073	trp2 segment 17	90 nts
SEQ ID NO: 1074	Polypeptide encoded by SEQ ID NO: 1073	30 aa
SEQ ID NO: 1075	trp2 segment 18	90 nts
SEQ ID NO: 1076	Polypeptide encoded by SEQ ID NO: 1075	30 aa
SEQ ID NO: 1077	trp2 segment 19	90 nts
SEQ ID NO: 1078	Polypeptide encoded by SEQ ID NO: 1077	30 aa

SEQUENCE ID	SEQUENCE	LENGTH
NUMBER		
SEQ ID NO: 1079	trp2 segment 20	90 nts
SEQ ID NO: 1080	Polypeptide encoded by SEQ ID NO: 1079	30 aa 、
SEQ ID NO: 1081	trp2 segment 21	90 nts
SEQ ID NO: 1082	Polypeptide encoded by SEQ ID NO: 1081	30 aa
SEQ ID NO: 1083	trp2 segment 22	90 nts
SEQ ID NO: 1084	Polypeptide encoded by SEQ ID NO: 1083	30 aa
SEQ ID NO: 1085	trp2 segment 23	90 nts
SEQ ID NO: 1086	Polypeptide encoded by SEQ ID NO: 1085	30 aa
SEQ ID NO: 1087	trp2 segment 24	90 nts
SEQ ID NO: 1088	Polypeptide encoded by SEQ ID NO: 1087	30 aa
SEQ ID NO: 1089	trp2 segment 25	90 nts
SEQ ID NO: 1090	Polypeptide encoded by SEQ ID NO: 1089	30 aa
SEQ ID NO: 1091	trp2 segment 26	90 nts
SEQ ID NO: 1092	Polypeptide encoded by SEQ ID NO: 1091	30 aa
SEQ ID NO: 1093	trp2 segment 27	90 nts
SEQ ID NO: 1094	Polypeptide encoded by SEQ ID NO: 1093	30 aa
SEQ ID NO: 1095	trp2 segment 28	90 nts
SEQ ID NO: 1096	Polypeptide encoded by SEQ ID NO: 1095	30 aa
SEQ ID NO: 1097	trp2 segment 29	90 nts
SEQ ID NO: 1098	Polypeptide encoded by SEQ ID NO: 1097	30 aa
SEQ ID NO: 1099	trp2 segment 30	90 nts
SEQ ID NO: 1100	Polypeptide encoded by SEQ ID NO: 1099	30 aa
SEQ ID NO: 1101	trp2 segment 31	90 nts
SEQ ID NO: 1102	Polypeptide encoded by SEQ ID NO: 1101	30 aa

SEQUENCE ID NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 1103	trp2 segment 32	90 nts
SEQ ID NO: 1104	Polypeptide encoded by SEQ ID NO: 1103	30 aa
SEQ ID NO: 1105	trp2 segment 33	90 nts
SEQ ID NO: 1106	Polypeptide encoded by SEQ ID NO: 1105	30 aa
SEQ ID NO: 1107	trp2 segment 34	84 nts
SEQ ID NO: 1108	Polypeptide encoded by SEQ ID NO: 1107	28 aa
SEQ ID NO: 1109	MC1R segment 1	90 nts
SEQ ID NO: 1110	Polypeptide encoded by SEQ ID NO: 1109	30 aa
SEQ ID NO: 1111	MC1R segment 2	90 nts
SEQ ID NO: 1112	Polypeptide encoded by SEQ ID NO: 1111	30 aa
SEQ ID NO: 1113	MC1R segment 3	90 nts
SEQ ID NO: 1114	Polypeptide encoded by SEQ ID NO: 1113	30 aa
SEQ ID NO: 1115	MC1R segment 4	90 nts
SEQ ID NO: 1116	Polypeptide encoded by SEQ ID NO: 1115	30 aa
SEQ ID NO: 1117	MC1R segment 5	90 nts
SEQ ID NO: 1118	Polypeptide encoded by SEQ ID NO: 1117	30 aa
SEQ ID NO: 1119	MC1R segment 6	90 nts
SEQ ID NO: 1120	Polypeptide encoded by SEQ ID NO: 1119	30 aa
SEQ ID NO: 1121	MC1R segment 7	90 nts
SEQ ID NO: 1122	Polypeptide encoded by SEQ ID NO: 1121	30 aa
SEQ ID NO: 1123	MC1R segment 8	90 nts
SEQ ID NO: 1124	Polypeptide encoded by SEQ ID NO: 1123	30 aa
SEQ ID NO: 1125	MC1R segment 9	90 nts
SEQ ID NO: 1126	Polypeptide encoded by SEQ ID NO: 1125	30 aa

SEQUENCE ID NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 1127	MC1R segment 10	90 nts
SEQ ID NO: 1128	Polypeptide encoded by SEQ ID NO: 1127	30 aa
SEQ ID NO: 1129	MC1R segment 11	90 nts
SEQ ID NO: 1130	Polypeptide encoded by SEQ ID NO: 1129	30 aa
SEQ ID NO: 1131	MC1R segment 12	90 nts
SEQ ID NO: 1132	Polypeptide encoded by SEQ ID NO: 1131	30 aa
SEQ ID NO: 1133	MC1R segment 13	90 nts
SEQ ID NO: 1134	Polypeptide encoded by SEQ ID NO: 1133	30 aa
SEQ ID NO: 1135	MC1R segment 14	90 nts
SEQ ID NO: 1136	Polypeptide encoded by SEQ ID NO: 1135	30 aa
SEQ ID NO: 1137	MC1R segment 15	90 nts
SEQ ID NO: 1138	Polypeptide encoded by SEQ ID NO: 1137	30 aa
SEQ ID NO: 1139	MC1R segment 16	90 nts
SEQ ID NO: 1140	Polypeptide encoded by SEQ ID NO: 1139	30 aa
SEQ ID NO: 1141	MC1R segment 17	90 nts
SEQ ID NO: 1142	Polypeptide encoded by SEQ ID NO: 1141	30 aa
SEQ ID NO: 1143	MC1R segment 18	90 nts
SEQ ID NO: 1144	Polypeptide encoded by SEQ ID NO: 1143	30 aa
SEQ ID NO: 1145	MC1R segment 19	90 nts
SEQ ID NO: 1146	Polypeptide encoded by SEQ ID NO: 1145	30 aa
SEQ ID NO: 1147	MC1R segment 20	90 nts
SEQ ID NO: 1148	Polypeptide encoded by SEQ ID NO: 1147	30 aa
SEQ ID NO: 1149	MC1R segment 21	63 nts
SEQ ID NO: 1150	Polypeptide encoded by SEQ ID NO: 1149	21 aa

SEQUENCE ID	SEQUENCE	LENGTH
NUMBER		
SEQ ID NO: 1151	MUC1F segment 1	90 nts
SEQ ID NO: 1152	Polypeptide encoded by SEQ ID NO: 1151	30 aa
SEQ ID NO: 1153	MUC1F segment 2	90 nts
SEQ ID NO: 1154	Polypeptide encoded by SEQ ID NO: 1153	30 aa
SEQ ID NO: 1155	MUC1F segment 3	90 nts
SEQ ID NO: 1156	Polypeptide encoded by SEQ ID NO: 1155	30 aa
SEQ ID NO: 1157	MUC1F segment 4	90 nts
SEQ ID NO: 1158	Polypeptide encoded by SEQ ID NO: 1157	30 aa
SEQ ID NO: 1159	MUC1F segment 5	90 nts
SEQ ID NO: 1160	Polypeptide encoded by SEQ ID NO: 1159	30 aa
SEQ ID NO: 1161	MUC1F segment 6	90 nts
SEQ ID NO: 1162	Polypeptide encoded by SEQ ID NO: 1161	30 aa
SEQ ID NO: 1163	MUC1F segment 7	90 nts
SEQ ID NO: 1164	Polypeptide encoded by SEQ ID NO: 1163	30 aa
SEQ ID NO: 1165	MUC1F segment 8	72 nts
SEQ ID NO: 1166	Polypeptide encoded by SEQ ID NO: 1165	24 aa
SEQ ID NO: 1167	MUC1R segment 1	90 nts
SEQ ID NO: 1168	Polypeptide encoded by SEQ ID NO: 1167	30 aa
SEQ ID NO: 1169	MUC1R segment 2	90 nts
SEQ ID NO: 1170	Polypeptide encoded by SEQ ID NO: 1169	30 aa
SEQ ID NO: 1171	MUC1R segment 3	90 nts
SEQ ID NO: 1172	Polypeptide encoded by SEQ ID NO: 1171	30 aa
SEQ ID NO: 1173	MUC1R segment 4	90 nts
SEQ ID NO: 1174	Polypeptide encoded by SEQ ID NO: 1173	30 aa

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SEQUENCE ID NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 1175	MUC1R segment 5	90 nts
SEQ ID NO: 1176	Polypeptide encoded by SEQ ID NO: 1175	30 aa
SEQ ID NO: 1177	MUC1R segment 6	90 nts
SEQ ID NO: 1178	Polypeptide encoded by SEQ ID NO: 1177	30 aa
SEQ ID NO: 1179	MUC1R segment 7	90 nts
SEQ ID NO: 1180	Polypeptide encoded by SEQ ID NO: 1179	30 aa
SEQ ID NO: 1181	MUC1R segment 8	90 nts
SEQ ID NO: 1182	Polypeptide encoded by SEQ ID NO: 1181	30 aa
SEQ ID NO: 1183	MUC1R segment 9	90 nts
SEQ ID NO: 1184	Polypeptide encoded by SEQ ID NO: 1183	30 aa
SEQ ID NO: 1185	MUC1R segment 10	90 nts
SEQ ID NO: 1186	Polypeptide encoded by SEQ ID NO: 1185	30 aa
SEQ ID NO: 1187	MUC1R segment 11	90 nts
SEQ ID NO: 1188	Polypeptide encoded by SEQ ID NO: 1187	30 aa
SEQ ID NO: 1189	MUC1R segment 12	90 nts
SEQ ID NO: 1190	Polypeptide encoded by SEQ ID NO: 1189	30 aa
SEQ ID NO: 1191	MUC1R segment 13	90 nts
SEQ ID NO: 1192	Polypeptide encoded by SEQ ID NO: 1191	30 aa
SEQ ID NO: 1193	MUC1R segment 14	90 nts
SEQ ID NO: 1194	Polypeptide encoded by SEQ ID NO: 1193	30 aa
SEQ ID NO: 1195	MUC1R segment 15	90 nts
SEQ ID NO: 1196	Polypeptide encoded by SEQ ID NO: 1195	30 aa
SEQ ID NO: 1197	MUC1R segment 16	90 nts
SEQ ID NO: 1198	Polypeptide encoded by SEQ ID NO: 1197	30 aa

SEQUENCE ID	SEQUENCE	LENGTH
NUMBER		
SEQ ID NO: 1199	MUC1R segment 17	90 nts
SEQ ID NO: 1200	Polypeptide encoded by SEQ ID NO: 1199	30 aa
SEQ ID NO: 1201	MUC1R segment 18	90 nts
SEQ ID NO: 1202	Polypeptide encoded by SEQ ID NO: 1201	30 aa
SEQ ID NO: 1203	MUC1R segment 19	90 nts
SEQ ID NO: 1204	Polypeptide encoded by SEQ ID NO: 1203	30 aa
SEQ ID NO: 1205	MUC1R segment 20	90 nts
SEQ ID NO: 1206	Polypeptide encoded by SEQ ID NO: 1205	30 aa
SEQ ID NO: 1207	MUC1R segment 21	48 nts
SEQ ID NO: 1208	Polypeptide encoded by SEQ ID NO: 1207	16 aa
SEQ ID NO: 1209	Differentiation Savine	16638 nts
SEQ ID NO: 1210	Polypeptide encoded by SEQ ID NO: 1209	5546 aa
SEQ ID NO: 1211	BAGE segment 1	90 nts
SEQ ID NO: 1212	Polypeptide encoded by SEQ ID NO: 1211	30 aa
SEQ ID NO: 1213	BAGE segment 2	90 nts
SEQ ID NO: 1214	Polypeptide encoded by SEQ ID NO: 1213	30 aa
SEQ ID NO: 1215	BAGE segment 3	51 nts
SEQ ID NO: 1216	Polypeptide encoded by SEQ ID NO: 1215	17 aa
SEQ ID NO: 1217	GAGE-1 segment 1	90 nts
SEQ ID NO: 1218	Polypeptide encoded by SEQ ID NO: 1217	30 aa.
SEQ ID NO: 1219	GAGE-1 segment 2	90 nts
SEQ ID NO: 1220	Polypeptide encoded by SEQ ID NO: 1219	30 aa
SEQ ID NO: 1221	GAGE-1 segment 3	90 nts
SEQ ID NO: 1222	Polypeptide encoded by SEQ ID NO: 1221	30 aa

SEQUENCE ID NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 1223	GAGE-1 segment 4	90 nts
SEQ ID NO: 1224	Polypeptide encoded by SEQ ID NO: 1223	30 aa
SEQ ID NO: 1225	GAGE-1 segment 5	90 nts
SEQ ID NO: 1226	Polypeptide encoded by SEQ ID NO: 1225	30 aa
SEQ ID NO: 1227	GAGE-1 segment 6	90 nts
SEQ ID NO: 1228	Polypeptide encoded by SEQ ID NO: 1227	30 aa
SEQ ID NO: 1229	GAGE-1 segment 7	90 nts
SEQ ID NO: 1230	Polypeptide encoded by SEQ ID NO: 1229	30 aa
SEQ ID NO: 1231	GAGE-1 segment 8	90 nts
SEQ ID NO: 1232	Polypeptide encoded by SEQ ID NO: 1231	30 aa
SEQ ID NO: 1233	GAGE-1 segment 9	66 nts
SEQ ID NO: 1234	Polypeptide encoded by SEQ ID NO: 1233	22 aa
SEQ ID NO: 1235	gp100ln4 segment 1	90 nts
SEQ ID NO: 1236	Polypeptide encoded by SEQ ID NO: 1235	30 aa
SEQ ID NO: 1237	gp100ln4 segment 2	90 nts
SEQ ID NO: 1238	Polypeptide encoded by SEQ ID NO: 1237	30 aa
SEQ ID NO: 1239	gp100ln4 segment 3	75 nts
SEQ ID NO: 1240	Polypeptide encoded by SEQ ID NO: 1239	25 aa
SEQ ID NO: 1241	MAGE-1 segment 1	90 nts
SEQ ID NO: 1242	Polypeptide encoded by SEQ ID NO: 1241	30 aa
SEQ ID NO: 1243	MAGE-1 segment 2	90 nts
SEQ ID NO: 1244	Polypeptide encoded by SEQ ID NO: 1243	30 aa
SEQ ID NO: 1245	MAGE-1 segment 3	90 nts
SEQ ID NO: 1246	Polypeptide encoded by SEQ ID NO: 1245	30 aa

SEQUENCE ID NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 1247	MAGE-1 segment 4	90 nts
SEQ ID NO: 1248	Polypeptide encoded by SEQ ID NO: 1247	30 aa
SEQ ID NO: 1249	MAGE-1 segment 5	90 nts
SEQ ID NO: 1250	Polypeptide encoded by SEQ ID NO: 1249	30 aa
SEQ ID NO: 1251	MAGE-1 segment 6	90 nts
SEQ ID NO: 1252	Polypeptide encoded by SEQ ID NO: 1251	30 aa
SEQ ID NO: 1253	MAGE-1 segment 7	90 nts
SEQ ID NO: 1254	Polypeptide encoded by SEQ ID NO: 1253	30 aa
SEQ ID NO: 1255	MAGE-1 segment 8	90 nts
SEQ ID NO: 1256	Polypeptide encoded by SEQ ID NO: 1255	30 aa
SEQ ID NO: 1257	MAGE-1 segment 9	90 nts
SEQ ID NO: 1258	Polypeptide encoded by SEQ ID NO: 1257	30 aa
SEQ ID NO: 1259	MAGE-1 segment 10	90 nts
SEQ ID NO: 1260	Polypeptide encoded by SEQ ID NO: 1259	30 aa
SEQ ID NO: 1261	MAGE-1 segment 11	90 nts
SEQ ID NO: 1262	Polypeptide encoded by SEQ ID NO: 1261	30 aa
SEQ ID NO: 1263	MAGE-1 segment 12	90 nts
SEQ ID NO: 1264	Polypeptide encoded by SEQ ID NO: 1263	30 aa
SEQ ID NO: 1265	MAGE-1 segment 13	90 nts
SEQ ID NO: 1266	Polypeptide encoded by SEQ ID NO: 1265	30 aa
SEQ ID NO: 1267	MAGE-1 segment 14	90 nts
SEQ ID NO: 1268	Polypeptide encoded by SEQ ID NO: 1267	30 aa
SEQ ID NO: 1269	MAGE-1 segment 15	90 nts
SEQ ID NO: 1270	Polypeptide encoded by SEQ ID NO: 1269	30 aa

SEQUENCE ID	SEQUENCE	LENGTH
NUMBER		
SEQ ID NO: 1271	MAGE-1 segment 16	90 nts
SEQ ID NO: 1272	Polypeptide encoded by SEQ ID NO: 1271	30 aa
SEQ ID NO: 1273	MAGE-1 segment 17	90 nts
SEQ ID NO: 1274	Polypeptide encoded by SEQ ID NO: 1273	30 aa
SEQ ID NO: 1275	MAGE-1 segment 18	90 nts
SEQ ID NO: 1276	Polypeptide encoded by SEQ ID NO: 1275	30 aa
SEQ ID NO: 1277	MAGE-1 segment 19	90 nts
SEQ ID NO: 1278	Polypeptide encoded by SEQ ID NO: 1277	30 aa
SEQ ID NO: 1279	MAGE-1 segment 20	84 nts
SEQ ID NO: 1280	Polypeptide encoded by SEQ ID NO: 1279	28 aa
SEQ ID NO: 1281	MAGE-3 segment 1	90 nts
SEQ ID NO: 1282	Polypeptide encoded by SEQ ID NO: 1281	30 aa
SEQ ID NO: 1283	MAGE-3 segment 2	90 nts
SEQ ID NO: 1284	Polypeptide encoded by SEQ ID NO: 1283	30 aa
SEQ ID NO: 1285	MAGE-3 segment 3	90 nts
SEQ ID NO: 1286	Polypeptide encoded by SEQ ID NO: 1285	30 aa
SEQ ID NO: 1287	MAGE-3 segment 4	90 nts
SEQ ID NO: 1288	Polypeptide encoded by SEQ ID NO: 1287	30 aa
SEQ ID NO: 1289	MAGE-3 segment 5	90 nts
SEQ ID NO: 1290	Polypeptide encoded by SEQ ID NO: 1289	30 aa
SEQ ID NO: 1291	MAGE-3 segment 6	90 nts
SEQ ID NO: 1292	Polypeptide encoded by SEQ ID NO: 1291	30 aa
SEQ ID NO: 1293	MAGE-3 segment 7	90 nts
SEQ ID NO: 1294	Polypeptide encoded by SEQ ID NO: 1293	30 aa

SEQUENCE ID	SEQUENCE	LENGTH
NUMBER		
SEQ ID NO: 1295	MAGE-3 segment 8	90 nts
SEQ ID NO: 1296	Polypeptide encoded by SEQ ID NO: 1295	30 aa
SEQ ID NO: 1297	MAGE-3 segment 9	90 nts
SEQ ID NO: 1298	Polypeptide encoded by SEQ ID NO: 1297	30 aa
SEQ ID NO: 1299	MAGE-3 segment 10	90 nts
SEQ ID NO: 1300	Polypeptide encoded by SEQ ID NO: 1299	30 aa
SEQ ID NO: 1301	MAGE-3 segment 11	90 nts
SEQ ID NO: 1302	Polypeptide encoded by SEQ ID NO: 1301	30 aa
SEQ ID NO: 1303	MAGE-3 segment 12	90 nts
SEQ ID NO: 1304	Polypeptide encoded by SEQ ID NO: 1303	30 aa
SEQ ID NO: 1305	MAGE-3 segment 13	90 nts
SEQ ID NO: 1306	Polypeptide encoded by SEQ ID NO: 1305	30 aa
SEQ ID NO: 1307	MAGE-3 segment 14	90 nts
SEQ ID NO: 1308	Polypeptide encoded by SEQ ID NO: 1307	30 aa
SEQ ID NO: 1309	MAGE-3 segment 15	90 nts
SEQ ID NO: 1310	Polypeptide encoded by SEQ ID NO: 1309	30 aa
SEQ ID NO: 1311	MAGE-3 segment 16	90 nts
SEQ ID NO: 1312	Polypeptide encoded by SEQ ID NO: 1311	30 aa
SEQ ID NO: 1313	MAGE-3 segment 17	90 nts
SEQ ID NO: 1314	Polypeptide encoded by SEQ ID NO: 1313	30 aa
SEQ ID NO: 1315	MAGE-3 segment 18	90 nts
SEQ ID NO: 1316	Polypeptide encoded by SEQ ID NO: 1315	30 aa
SEQ ID NO: 1317	MAGE-3 segment 19	90 nts
SEQ ID NO: 1318	Polypeptide encoded by SEQ ID NO: 1317	30 aa

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SEQUENCE ID NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 1319	MAGE-3 segment 20	90 nts
SEQ ID NO: 1320	Polypeptide encoded by SEQ ID NO: 1319	30 aa
SEQ ID NO: 1321	MAGE-3 segment 21	54 nts
SEQ ID NO: 1322	Polypeptide encoded by SEQ ID NO: 1321	18 aa
SEQ ID NO: 1323	PRAME segment 1	90 nts
SEQ ID NO: 1324	Polypeptide encoded by SEQ ID NO: 1323	30 aa
SEQ ID NO: 1325	PRAME segment 2	90 nts
SEQ ID NO: 1326	Polypeptide encoded by SEQ ID NO: 1325	30 aa
SEQ ID NO: 1327	PRAME segment 3	90 nts
SEQ ID NO: 1328	Polypeptide encoded by SEQ ID NO: 1327	30 aa
SEQ ID NO: 1329	PRAME segment 4	90 nts
SEQ ID NO: 1330	Polypeptide encoded by SEQ ID NO: 1329	30 aa
SEQ ID NO: 1331	PRAME segment 5	90 nts
SEQ ID NO: 1332	Polypeptide encoded by SEQ ID NO: 1331	30 aa
SEQ ID NO: 1333	PRAME segment 6	90 nts
SEQ ID NO: 1334	Polypeptide encoded by SEQ ID NO: 1333	30 aa
SEQ ID NO: 1335	PRAME segment 7	90 nts
SEQ ID NO: 1336	Polypeptide encoded by SEQ ID NO: 1335	30 aa
SEQ ID NO: 1337	PRAME segment 8	90 nts
SEQ ID NO: 1338	Polypeptide encoded by SEQ ID NO: 1337	30 aa
SEQ ID NO: 1339	PRAME segment 9	90 nts
SEQ ID NO: 1340	Polypeptide encoded by SEQ ID NO: 1339	30 aa
SEQ ID NO: 1341	PRAME segment 10	90 nts
SEQ ID NO: 1342	Polypeptide encoded by SEQ ID NO: 1341	30 aa

SEQUENCE ID NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 1343	PRAME segment 11	90 nts
SEQ ID NO: 1344	Polypeptide encoded by SEQ ID NO: 1343	30 aa
SEQ ID NO: 1345	PRAME segment 12	90 nts
SEQ ID NO: 1346	Polypeptide encoded by SEQ ID NO: 1345	30 aa
SEQ ID NO: 1347	PRAME segment 13	90 nts
SEQ ID NO: 1348	Polypeptide encoded by SEQ ID NO: 1347	30 aa
SEQ ID NO: 1349	PRAME segment 14	90 nts
SEQ ID NO: 1350	Polypeptide encoded by SEQ ID NO: 1349	30 aa
SEQ ID NO: 1351	PRAME segment 15	90 nts
SEQ ID NO: 1352	Polypeptide encoded by SEQ ID NO: 1351	30 aa
SEQ ID NO: 1353	PRAME segment 16.	90 nts
SEQ ID NO: 1354	Polypeptide encoded by SEQ ID NO: 1353	30 aa
SEQ ID NO: 1355	PRAME segment 17	90 nts
SEQ ID NO: 1356	Polypeptide encoded by SEQ ID NO: 1355	30 aa
SEQ ID NO: 1357	PRAME segment 18	90 nts
SEQ ID NO: 1358	Polypeptide encoded by SEQ ID NO: 1357	30 aa
SEQ ID NO: 1359	PRAME segment 19	90 nts
SEQ ID NO: 1360	Polypeptide encoded by SEQ ID NO: 1359	30 aa
SEQ ID NO: 1361	PRAME segment 20	90 nts
SEQ ID NO: 1362	Polypeptide encoded by SEQ ID NO: 1361	30 aa
SEQ ID NO: 1363	PRAME segment 21	90 nts
SEQ ID NO: 1364	Polypeptide encoded by SEQ ID NO: 1363	30 aa
SEQ ID NO: 1365	PRAME segment 22	90 nts
SEQ ID NO: 1366	Polypeptide encoded by SEQ ID NO: 1365	30 aa

SEQUENCE ID NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 1367	PRAME segment 23	90 nts
SEQ ID NO: 1368	Polypeptide encoded by SEQ ID NO: 1367	30 aa
SEQ ID NO: 1369	PRAME segment 24	90 nts
SEQ ID NO: 1370	Polypeptide encoded by SEQ ID NO: 1369	30 aa
SEQ ID NO: 1371	PRAME segment 25	90 nts
SEQ ID NO: 1372	Polypeptide encoded by SEQ ID NO: 1371	30 aa
SEQ ID NO: 1373	PRAME segment 26	90 nts
SEQ ID NO: 1374	Polypeptide encoded by SEQ ID NO: 1373	30 aa
SEQ ID NO: 1375	PRAME segment 27	90 nts
SEQ ID NO: 1376	Polypeptide encoded by SEQ ID NO: 1375	30 aa
SEQ ID NO: 1377	PRAME segment 28	90 nts
SEQ ID NO: 1378	Polypeptide encoded by SEQ ID NO: 1377	30 aa
SEQ ID NO: 1379	PRAME segment 29	90 nts
SEQ ID NO: 1380	Polypeptide encoded by SEQ ID NO: 1379	30 aa
SEQ ID NO: 1381	PRAME segment 30	90 nts
SEQ ID NO: 1382	Polypeptide encoded by SEQ ID NO: 1381	30 aa
SEQ ID NO: 1383	PRAME segment 31	90 nts
SEQ ID NO: 1384	Polypeptide encoded by SEQ ID NO: 1383	30 aa
SEQ ID NO: 1385	PRAME segment 32	90 nts _.
SEQ ID NO: 1386	Polypeptide encoded by SEQ ID NO: 1385	30 aa
SEQ ID NO: 1387	PRAME segment 33	90 nts
SEQ ID NO: 1388	Polypeptide encoded by SEQ ID NO: 1387	30 aa
SEQ ID NO: 1389	PRAME segment 34	54 nts
SEQ ID NO: 1390	Polypeptide encoded by SEQ ID NO: 1389	18 aa

SEQUENCE ID NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 1391	TRP2IN2 segment 1	90 nts
SEQ ID NO: 1392	Polypeptide encoded by SEQ ID NO: 1391	30 aa
SEQ ID NO: 1393	TRP2IN2 segment 2	90 nts
SEQ ID NO: 1394	Polypeptide encoded by SEQ ID NO: 1393	30 aa
SEQ ID NO: 1395	TRP2IN2 segment 3	84 nts
SEQ ID NO: 1396	Polypeptide encoded by SEQ ID NO: 1395	28 aa
SEQ ID NO: 1397	NYNSO1a segment 1	90 nts
SEQ ID NO: 1398	Polypeptide encoded by SEQ ID NO: 1397	30 aa
SEQ ID NO: 1399	NYNSO1a segment 2	90 nts
SEQ ID NO: 1400	Polypeptide encoded by SEQ ID NO: 1399	30 aa
SEQ ID NO: 1401	NYNSO1a segment 3	90 nts
SEQ ID NO: 1402	Polypeptide encoded by SEQ ID NO: 1401	30 aa
SEQ ID NO: 1403	NYNSO1a segment 4	90 nts
SEQ ID NO: 1404	Polypeptide encoded by SEQ ID NO: 1403	30 aa
SEQ ID NO: 1405	NYNSO1a segment 5	90 nts
SEQ ID NO: 1406	Polypeptide encoded by SEQ ID NO: 1405	30 aa
SEQ ID NO: 1407	NYNSO1a segment 6	90 nts
SEQ ID NO: 1408	Polypeptide encoded by SEQ ID NO: 1407	30 aa
SEQ ID NO: 1409	NYNSO1a segment 7	90 nts
SEQ ID NO: 1410	Polypeptide encoded by SEQ ID NO: 1409	30 aa
SEQ ID NO: 1411	NYNSO1a segment 8	90 nts
SEQ ID NO: 1412	Polypeptide encoded by SEQ ID NO: 1411	30 aa
SEQ ID NO: 1413	NYNSO1a segment 9	90 nts
SEQ ID NO: 1414	Polypeptide encoded by SEQ ID NO: 1413	30 aa

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SEQUENCE ID NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 1415	NYNSO1a segment 10	90 nts
SEQ ID NO: 1416	Polypeptide encoded by SEQ ID NO: 1415	30 aa
SEQ ID NO: 1417	NYNSO1a segment 11	90 nts
SEQ ID NO: 1418	Polypeptide encoded by SEQ ID NO: 1417	30 aa
SEQ ID NO: 1419	NYNSO1a segment 12	57 nts
SEQ ID NO: 1420	Polypeptide encoded by SEQ ID NO: 1419	19 aa
SEQ ID NO: 1421	NYNSO1b segment 1	90 nts
SEQ ID NO: 1422	Polypeptide encoded by SEQ ID NO: 1421	30 aa
SEQ ID NO: 1423	NYNSO1b segment 2	90 nts
SEQ ID NO: 1424	Polypeptide encoded by SEQ ID NO: 1423	30 aa
SEQ ID NO: 1425	NYNSO1b segment 3	90 nts
SEQ ID NO: 1426	Polypeptide encoded by SEQ ID NO: 1425	30 aa
SEQ ID NO: 1427	NYNSO1b segment 4	51 nts
SEQ ID NO: 1428	Polypeptide encoded by SEQ ID NO: 1427	
SEQ ID NO: 1429	LAGE1 segment 1	90 nts
SEQ ID NO: 1430	Polypeptide encoded by SEQ ID NO: 1429	30 aa
SEQ ID NO: 1431	LAGE1 segment 2	90 nts
SEQ ID NO: 1432	Polypeptide encoded by SEQ ID NO: 1431	30 aa
SEQ ID NO: 1433	LAGE1 segment 3	90 nts _.
SEQ ID NO: 1434	Polypeptide encoded by SEQ ID NO: 1433	30 aa
SEQ ID NO: 1435	LAGE1 segment 4	90 nts
SEQ ID NO: 1436	Polypeptide encoded by SEQ ID NO: 1435	30 aa
SEQ ID NO: 1437	LAGE1 segment 5	90 nts
SEQ ID NO: 1438	Polypeptide encoded by SEQ ID NO: 1437	30 aa

SEQUENCE ID NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 1439	LAGE1 segment 6	90 nts
SEQ ID NO: 1440	Polypeptide encoded by SEQ ID NO: 1439	30 aa
SEQ ID NO: 1441	LAGE1 segment 7	90 nts
SEQ ID NO: 1442	Polypeptide encoded by SEQ ID NO: 1441	30 aa
SEQ ID NO: 1443	LAGE1 segment 8	90 nts
SEQ ID NO: 1444	Polypeptide encoded by SEQ ID NO: 1443	30 aa
SEQ ID NO: 1445	LAGE1 segment 9	90 nts
SEQ ID NO: 1446	Polypeptide encoded by SEQ ID NO: 1445	30 aa
SEQ ID NO: 1447	LAGE1 segment 10	90 nts
SEQ ID NO: 1448	Polypeptide encoded by SEQ ID NO: 1447	30 aa
SEQ ID NO: 1449	LAGE1 segment 11	90 nts
SEQ ID NO: 1450	Polypeptide encoded by SEQ ID NO: 1449	30 aa
SEQ ID NO: 1451	LAGE1 segment 12	57 nts
SEQ ID NO: 1452	Polypeptide encoded by SEQ ID NO: 1451	19 aa
SEQ ID NO: 1453	Melanoma cancer specific Savine	10623 nts
SEQ ID NO: 1454	Polypeptide encoded by SEQ ID NO: 1453	3541 aa
SEQ ID NO: 1455	Figure 16 A1S1 99mer	99 nts
SEQ ID NO: 1456	Figure 16 A1S2 100mer	100 nts
SEQ ID NO: 1457	Figure 16 A1S3 100mer	100 nts
SEQ ID NO: 1458	Figure 16 A1S4 100mer	100 nts
SEQ ID NO: 1459	Figure 16 A1S5 100mer	100 nts
SEQ ID NO: 1460	Figure 16 A1S6 99mer	99 nts
SEQ ID NO: 1461	Figure 16 A1S7 97mer	99 nts
SEQ ID NO: 1462	Figure 16 A1S8 100mer	100 nts

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SEQUENCE ID NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 1463	Figure 16 A1S9 100mer	100 nts
SEQ ID NO: 1464	Figure 16 A1S10 75mer	76 nts
SEQ ID NO: 1465	Figure 16 A1F 20mer	20 nts
SEQ ID NO: 1466	Figure 16 A1R 20mer	20 nts
SEQ ID NO: 1467	Amino acid sequence of immunostimulatory domain of an invasin protein from <i>Yersinia</i> spp.	16 aa

DETAILED DESCRIPTION OF THE INVENTION

1. Definitions

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The articles "a" and "an" are used herein to refer to one or to more than one (i.e., to at least one) of the grammatical object of the article. By way of example, "an element" means one element or more than one element.

As used herein, the term "about" refers to a quantity, level, value, dimension, size, or amount that varies by as much as 30%, preferably by as much as 20%, and more preferably by as much as 10% to a reference quantity, level, value, dimension, size, or amount.

By "antigen-binding molecule" is meant a molecule that has binding affinity for a target antigen. It will be understood that this term extends to immunoglobulins, immunoglobulin fragments and non-immunoglobulin derived protein frameworks that exhibit antigen-binding activity.

The term "clade" as used herein refers to a hypothetical species of an organism and its descendants or a monophyletic group of organisms. Clades carry a definition, based on ancestry, and a diagnosis, based on synapomorphies. It should be noted that diagnoses of clades could change while definitions do not.

Throughout this specification, unless the context requires otherwise, the words "comprise", "comprises" and "comprising" will be understood to imply the inclusion of a stated step or element or group of steps or elements but not the exclusion of any other step or element or group of steps or elements.

By "expression vector" is meant any autonomous genetic element capable of directing the synthesis of a protein encoded by the vector. Such expression vectors are known by practitioners in the art.

As used herein, the term "function" refers to a biological, enzymatic, or therapeutic function.

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"Homology" refers to the percentage number of amino acids that are identical or constitute conservative substitutions as defined in Table B infra. Homology may be determined using sequence comparison programs such as GAP (Deveraux et al. 1984, Nucleic Acids Research 12, 387-395). In this way, sequences of a similar or substantially different length to those cited herein might be compared by insertion of gaps into the alignment, such gaps being determined, for example, by the comparison algorithm used by GAP.

To enhance an immune response ("immunoenhancement"), as is well-known in the art, means to increase an animal's capacity to respond to foreign or disease-specific antigens (e.g., cancer antigens) i.e., those cells primed to attack such antigens are increased in number, activity, and ability to detect and destroy the those antigens. Strength of immune response is measured by standard tests including: direct measurement of peripheral blood lymphocytes by means known to the art; natural killer cell cytotoxicity assays (see, e.g., Provinciali M. et al (1992, J. Immunol. Meth. 155: 19-24), cell proliferation assays (see, e.g., Vollenweider, I. and Groseurth, P. J. (1992, J. Immunol. Meth. 149: 133-135), immunoassays of immune cells and subsets (see, e.g., Loeffler, D. A., et al. (1992, Cytom. 13: 169-174); Rivoltini, L., et al. (1992, Can. Immunol. Immunother. 34: 241-251); or skin tests for cell-mediated immunity (see, e.g., Chang, A. E. et al (1993, Cancer Res. 53: 1043-1050). Any statistically significant increase in strength of immune response as measured by the foregoing tests is considered "enhanced immune response" "immunoenhancement" or "immunopotentiation" as used herein. Enhanced immune response is also indicated by physical manifestations such as fever and inflammation, as well as healing of systemic and local infections, and reduction of symptoms in disease, i.e., decrease in tumour size, alleviation of symptoms of a disease or condition including, but not restricted to, leprosy, tuberculosis, malaria, naphthous ulcers, herpetic and papillomatous warts, gingivitis, artherosclerosis, the concomitants of AIDS such as Kaposi's sarcoma, bronchial infections, and the like. Such physical manifestations define response" "immunoenhancement" also "enhanced immune or "immunopotentiation" as used herein.

Reference herein to "immuno-interactive" includes reference to any interaction, reaction, or other form of association between molecules and in particular where one of the molecules is, or mimics, a component of the immune system.

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By "isolated" is meant material that is substantially or essentially free from components that normally accompany it in its native state.

By "modulating" is meant increasing or decreasing, either directly or indirectly, an immune response against a target antigen of a member selected from the group consisting of a cancer and an organism, preferably a pathogenic organism.

By "natural gene" is meant a gene that naturally encodes a protein.

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The term "natural polypeptide" as used herein refers to a polypeptide that exists in nature.

By "obtained from" is meant that a sample such as, for example, a polynucleotide extract or polypeptide extract is isolated from, or derived from, a particular source of the host. For example, the extract can be obtained from a tissue or a biological fluid isolated directly from the host.

The term "oligonucleotide" as used herein refers to a polymer composed of a multiplicity of nucleotide residues (deoxyribonucleotides or ribonucleotides, or related structural variants or synthetic analogues thereof) linked via phosphodiester bonds (or related structural variants or synthetic analogues thereof). Thus, while the term "oligonucleotide" typically refers to a nucleotide polymer in which the nucleotide residues and linkages between them are naturally occurring, it will be understood that the term also includes within its scope various analogues including, but not restricted to, peptide nucleic acids (PNAs), phosphoramidates, phosphorothioates, methyl phosphonates, 2-O-methyl ribonucleic acids, and the like. The exact size of the molecule can vary depending on the particular application. An oligonucleotide is typically rather short in length, generally from about 10 to 30 nucleotide residues, but the term can refer to molecules of any length, although the term "polynucleotide" or "nucleic acid" is typically used for large oligonucleotides.

By "operably linked" is meant that transcriptional and translational regulatory polynucleotides are positioned relative to a polypeptide-encoding polynucleotide in such a manner that the polynucleotide is transcribed and the polypeptide is translated.

The term "parent polypeptide" as used herein typically refers to a polypeptide encoded by a natural gene. However, it is possible that the parent polypeptide corresponds to a protein that is not naturally-occurring but has been engineered using recombinant techniques. In this instance, a polynucleotide encoding the parent polypeptide may comprise different but synonymous codons relative to a natural gene encoding the same polypeptide. Alternatively, the parent polypeptide may not correspond to a natural polypeptide sequence. For example, the parent polypeptide may comprise one or more consensus sequences common to a plurality of polypeptides.

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The term "patient" refers to patients of human or other mammal and includes any individual it is desired to examine or treat using the methods of the invention. However, it will be understood that "patient" does not imply that symptoms are present. Suitable mammals that fall within the scope of the invention include, but are not restricted to, primates, livestock animals (e.g., sheep, cows, horses, donkeys, pigs), laboratory test animals (e.g., rabbits, mice, rats, guinea pigs, hamsters), companion animals (e.g., cats, dogs) and captive wild animals (e.g., foxes, deer, dingoes).

By "pharmaceutically-acceptable carrier" is meant a solid or liquid filler, diluent or encapsulating substance that can be safely used in topical or systemic administration to a mammal.

"Polypeptide", "peptide" and "protein" are used interchangeably herein to refer to a polymer of amino acid residues and to variants and synthetic analogues of the same. Thus, these terms apply to amino acid polymers in which one or more amino acid residues is a synthetic non-naturally occurring amino acid, such as a chemical analogue of a corresponding naturally occurring amino acid, as well as to naturally-occurring amino acid polymers.

The term "polynucleotide" or "nucleic acid" as used herein designates mRNA, RNA, cRNA, cDNA or DNA. The term typically refers to oligonucleotides greater than 30 nucleotide residues in length.

By "primer" is meant an oligonucleotide which, when paired with a strand of DNA, is capable of initiating the synthesis of a primer extension product in the presence of a suitable polymerising agent. The primer is preferably single-stranded for maximum

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efficiency in amplification but can alternatively be double-stranded. A primer must be sufficiently long to prime the synthesis of extension products in the presence of the polymerisation agent. The length of the primer depends on many factors, including application, temperature to be employed, template reaction conditions, other reagents, and source of primers. For example, depending on the complexity of the target sequence, the oligonucleotide primer typically contains 15 to 35 or more nucleotide residues, although it can contain fewer nucleotide residues. Primers can be large polynucleotides, such as from about 35 nucleotides to several kilobases or more. Primers can be selected to be "substantially complementary" to the sequence on the template to which it is designed to hybridise and serve as a site for the initiation of synthesis. By "substantially complementary", it is meant that the primer is sufficiently complementary to hybridise with a target polynucleotide. Preferably, the primer contains no mismatches with the template to which it is designed to hybridise but this is not essential. For example, noncomplementary nucleotide residues can be attached to the 5' end of the primer, with the remainder of the primer sequence being complementary to the template. Alternatively, non-complementary nucleotide residues or a stretch of non-complementary nucleotide residues can be interspersed into a primer, provided that the primer sequence has sufficient complementarity with the sequence of the template to hybridise therewith and thereby form a template for synthesis of the extension product of the primer.

"Probe" refers to a molecule that binds to a specific sequence or sub-sequence or other moiety of another molecule. Unless otherwise indicated, the term "probe" typically refers to a polynucleotide probe that binds to another polynucleotide, often called the "target polynucleotide", through complementary base pairing. Probes can bind target polynucleotides lacking complete sequence complementarity with the probe, depending on the stringency of the hybridisation conditions. Probes can be labelled directly or indirectly.

By "recombinant polypeptide" is meant a polypeptide made using recombinant techniques, i.e., through the expression of a recombinant or synthetic polynucleotide.

Terms used to describe sequence relationships between two or more polynucleotides or polypeptides include "reference sequence", "comparison window", "sequence identity", "percentage of sequence identity" and "substantial identity". A "reference sequence" is at least 12 but frequently 15 to 18 and often at least 25 monomer

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units, inclusive of nucleotides and amino acid residues, in length. Because two polynucleotides may each comprise (1) a sequence (i.e., only a portion of the complete polynucleotide sequence) that is similar between the two polynucleotides, and (2) a sequence that is divergent between the two polynucleotides, sequence comparisons between two (or more) polynucleotides are typically performed by comparing sequences of the two polynucleotides over a "comparison window" to identify and compare local regions of sequence similarity. A "comparison window" refers to a conceptual segment of at least 50 contiguous positions, usually about 50 to about 100, more usually about 100 to about 150 in which a sequence is compared to a reference sequence of the same number of contiguous positions after the two sequences are optimally aligned. The comparison window may comprise additions or deletions (i.e., gaps) of about 20% or less as compared to the reference sequence (which does not comprise additions or deletions) for optimal alignment of the two sequences. Optimal alignment of sequences for aligning a comparison window may be conducted by computerised implementations of algorithms (GAP, BESTFIT, FASTA, and TFASTA in the Wisconsin Genetics Software Package Release 7.0, Genetics Computer Group, 575 Science Drive Madison, WI, USA) or by inspection and the best alignment (i.e., resulting in the highest percentage homology over the comparison window) generated by any of the various methods selected. Reference also may be made to the BLAST family of programs as for example disclosed by Altschul et al., 1997, Nucl. Acids Res. 25:3389. A detailed discussion of sequence analysis can be found in Unit 19.3 of Ausubel et al., "Current Protocols in Molecular Biology", John Wiley & Sons Inc, 1994-1998, Chapter 15.

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The term "sequence identity" as used herein refers to the extent that sequences are identical on a nucleotide-by-nucleotide basis or an amino acid-by-amino acid basis over a window of comparison. Thus, a "percentage of sequence identity" is calculated by comparing two optimally aligned sequences over the window of comparison, determining the number of positions at which the identical nucleic acid base (e.g., A, T, C, G, I) or the identical amino acid residue (e.g., Ala, Pro, Ser, Thr, Gly, Val, Leu, Ile, Phe, Tyr, Trp, Lys, Arg, His, Asp, Glu, Asn, Gln, Cys and Met) occurs in both sequences to yield the number of matched positions, dividing the number of matched positions by the total number of positions in the window of comparison (i.e., the window size), and multiplying the result by 100 to yield the percentage of sequence identity. For the purposes of the present

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invention, "sequence identity" will be understood to mean the "match percentage" calculated by the DNASIS computer program (Version 2.5 for windows; available from Hitachi Software engineering Co., Ltd., South San Francisco, California, USA) using standard defaults as used in the reference manual accompanying the software.

The term "synthetic polynucleotide" as used herein refers to a polynucleotide formed in vitro by the manipulation of a polynucleotide into a form not normally found in nature. For example, the synthetic polynucleotide can be in the form of an expression vector. Generally, such expression vectors include transcriptional and translational regulatory polynucleotide operably linked to the polynucleotide.

The term "synonymous codon" as used herein refers to a codon having a different nucleotide sequence than another codon but encoding the same amino acid as that other codon.

By "translational efficiency" is meant the efficiency of a cell's protein synthesis machinery to incorporate the amino acid encoded by a codon into a nascent polypeptide chain. This efficiency can be evidenced, for example, by the rate at which the cell is able to synthesise the polypeptide from an RNA template comprising the codon, or by the amount of the polypeptide synthesised from such a template.

By "vector" is meant a polynucleotide molecule, preferably a DNA molecule derived, for example, from a plasmid, bacteriophage, yeast or virus, into which a polynucleotide can be inserted or cloned. A vector preferably contains one or more unique restriction sites and can be capable of autonomous replication in a defined host cell including a target cell or tissue or a progenitor cell or tissue thereof, or be integrable with the genome of the defined host such that the cloned sequence is reproducible. Accordingly, the vector can be an autonomously replicating vector, i.e., a vector that exists as an extrachromosomal entity, the replication of which is independent of chromosomal replication, e.g., a linear or closed circular plasmid, an extrachromosomal element, a minichromosome, or an artificial chromosome. The vector can contain any means for assuring self-replication. Alternatively, the vector can be one which, when introduced into the host cell, is integrated into the genome and replicated together with the chromosome(s) into which it has been integrated. A vector system can comprise a single vector or plasmid, two or more vectors or plasmids, which together contain the total DNA to be introduced

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into the genome of the host cell, or a transposon. The choice of the vector will typically depend on the compatibility of the vector with the host cell into which the vector is to be introduced. In the present case, the vector is preferably a viral or viral-derived vector, which is operably functional in animal and preferably mammalian cells. Such vector may be derived from a poxvirus, an adenovirus or yeast. The vector can also include a selection marker such as an antibiotic resistance gene that can be used for selection of suitable transformants. Examples of such resistance genes are known to those of skill in the art and include the *nptIII* gene that confers resistance to the antibiotics kanamycin and G418 (Geneticin®) and the *hph* gene which confers resistance to the antibiotic hygromycin B.

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2. Synthetic polypeptides

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The inventors have surprisingly discovered that the structure of a parent polypeptide can be disrupted sufficiently to impede, abrogate or otherwise alter at least one function of the parent polypeptide, while simultaneously minimising the destruction of potentially useful epitopes that are present in the parent polypeptide, by fusing, coupling or otherwise linking together different segments of the parent polypeptide in a different relationship relative to their linkage in the parent polypeptide. As a result of this change in relationship, the sequence of the linked segments in the resulting synthetic polypeptide is different to a sequence contained within the parent polypeptide. The synthetic polypeptides of the invention are useful as immunopotentiating agents, and are referred to elsewhere in the specification as scrambled antigen vaccines, super attenuated vaccines or "Savines".

Thus, the invention broadly resides in a synthetic polypeptide comprising a plurality of different segments of at least one parent polypeptide, wherein said segments are linked together in a different relationship relative to their linkage in the at least one parent polypeptide.

It is preferable but not essential that the segments in said synthetic polypeptide are linked sequentially in a different order or arrangement relative to that of corresponding segments in said at least one parent polypeptide. For example, in the case of a parent polypeptide that comprises three contiguous or overlapping segments A-B-C-D, these segments may be linked in 23 other possible orders to form a synthetic polypeptide. These orders may be selected from the group consisting of: A-B-D-C, A-C-B-D, A-C-D-B, A-D-B-C, A-D-C-B, B-A-C-D, B-A-D-C, B-C-A-D, B-C-D-A, B-D-A-C, B-D-C-A, C-A-B-D, C-A-D-B, C-B-A-D, C-B-D-A, C-D-B-A, C-D-B-A, D-A-B-C, D-B-A-C, D-B-C-A, D-C-A-B, and D-C-B-A. Although the rearrangement of the segments is preferably random, it is especially preferable to exclude or otherwise minimise rearrangements that result in complete or partial reassembly of the parent sequence (e.g., ADBC, BACD, DABC). It will be appreciated, however, that the probability of such complete or partial reassembly diminishes as the number of segments for rearrangement increases.

The order of the segments is suitably shuffled, reordered or otherwise rearranged relative to the order in which they exist in the parent polypeptide so that the structure of the polypeptide is disrupted sufficiently to impede, abrogate or otherwise alter at least one

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function associated with the parent polypeptide. Preferably, the segments of the parent polypeptide are randomly rearranged in the synthetic polypeptide.

The parent polypeptide is suitably a polypeptide that is associated with a disease or condition. For example, the parent polypeptide may be a polypeptide expressed by a pathogenic organism or a cancer. Alternatively, the parent polypeptide can be a self peptide related to an autoimmune disease including, but are not limited to, diseases such as diabetes (e.g., juvenile diabetes), multiple sclerosis, rheumatoid arthritis, myasthenia gravis, atopic dermatitis, and psoriasis and ankylosing spondylitis. Accordingly, the synthetic molecules of the present invention may also have utility for the induction of tolerance in a subject afflicted with an autoimmune disease or condition or with an allergy or other condition to which tolerance is desired. For example tolerance may be induced by contacting an immature dendritic cell of the individual to be treated with a synthetic polypeptide of the invention or by expressing in an immature dendritic cell a synthetic polynucleotide of the invention. Tolerance may also be induced against antigens causing allergic responses (e.g., asthma, hay fever). In this case, the parent polypeptide is suitably an allergenic protein including, but not restricted to, house-dust-mite allergenic proteins as for example described by Thomas and Smith (1998, Allergy, 53(9): 821-832).

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The pathogenic organism includes, but is not restricted to, yeast, a virus, a bacterium, and a parasite. Any natural host of the pathogenic organism is contemplated by the present invention and includes, but is not limited to, mammals, avians and fish. In a preferred embodiment, the pathogenic organism is a virus, which may be an RNA virus or a DNA virus. Preferably, the RNA virus is Human Immunodeficiency Virus (HIV), Poliovirus, and Influenza virus, Rous sarcoma virus, or a Flavivirus such as Japanese encephalitis virus. In a preferred embodiment, the RNA virus is a Hepatitis virus including, but not limited to, Hepatitis strains A, B and C. Suitably, the DNA virus is a Herpesvirus including, but not limited to, Herpes simplex virus, Epstein-Barr virus, Cytomegalovirus and Parvovirus. In a preferred embodiment, the virus is HIV and the parent polypeptide is suitably selected from env, gag, pol, vif, vpr, tat, rev, vpu and nef, or combination thereof. In an alternate preferred embodiment, the virus is Hepatitis C1a virus and the parent polypeptide is the Hepatitis C1a virus polyprotein.

In another embodiment, the pathogenic organism is a bacterium, which includes, but is not restricted to, *Neisseria* species, *Meningococcal* species, *Haemophilus* species *Salmonella* species, *Streptococcal* species, *Legionella* species and *Mycobacterium* species.

In yet another embodiment, the pathogenic organism is a parasite, which includes, but is not restricted to, *Plasmodium* species, *Schistosoma* species, *Leishmania* species, *Trypanosoma* species, *Toxoplasma* species and *Giardia* species.

Any cancer or tumour is contemplated by the present invention. For example, the cancer or tumour includes, but is not restricted to, melanoma, lung cancer, breast cancer, cervical cancer, prostate cancer, colon cancer, pancreatic cancer, stomach cancer, bladder cancer, kidney cancer, post transplant lymphoproliferative disease (PTLD), Hodgkin's Lymphoma and the like. Preferably, the cancer or tumour relates to melanoma. In a preferred embodiment of this type, the parent polypeptide is a melanocyte differentiation antigen which is suitably selected from gp100, MART, TRP-1, Tyros, TRP2, MC1R, MUC1F, MUC1R or a combination thereof. In an alternate preferred embodiment of this type, the parent polypeptide is a melanoma-specific antigen which is suitably selected from BAGE, GAGE-1, gp100In4, MAGE-1, MAGE-3, PRAME, TRP2IN2, NYNSO1a, NYNSO1b, LAGE1 or a combination thereof.

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In a preferred embodiment, the segments are selected on the basis of size. A segment according to the invention may be of any suitable size that can be utilised to elicit an immune response against an antigen encoded by the parent polypeptide. A number of factors can influence the choice of segment size. For example, the size of a segment should be preferably chosen such that it includes, or corresponds to the size of, T cell epitopes and their processing requirement. Practitioners in the art will recognise that class I-restricted T cell epitopes can be between 8 and 10 amino acids in length and if placed next to unnatural flanking residues, such epitopes can generally require 2 to 3 natural flanking amino acids to ensure that they are efficiently processed and presented. Class II-restricted T cell epitopes can range between 12 and 25 amino acids in length and may not require natural flanking residues for efficient proteolytic processing although it is believed that natural flanking residues may play a role. Another important feature of class II-restricted epitopes is that they generally contain a core of 9-10 amino acids in the middle which bind specifically to class II MHC molecules with flanking sequences either side of this core

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stabilising binding by associating with conserved structures on either side of class II MHC antigens in a sequence independent manner (Brown et al., 1993). Thus the functional region of class II-restricted epitopes is typically less than 15 amino acids long. The size of linear B cell epitopes and the factors effecting their processing, like class II-restricted epitopes, are quite variable although such epitopes are frequently smaller in size than 15 amino acids. From the foregoing, it is preferable, but not essential, that the size of the segment is at least 4 amino acids, preferably at least 7 amino acids, more preferably at least 12 amino acids, more preferably at least 20 amino acids and more preferably at least 30 amino acids. Suitably, the size of the segment is less than 2000 amino acids, more preferably less than 1000 amino acids, more preferably less than 500 amino acids, more preferably less than 200 amino acids, more preferably less than 100 amino acids, more preferably less than 80 amino acids and even more preferably less than 60 amino acids and still even more preferably less than 40 amino acids. In this regard, it is preferable that the size of the segments is as small as possible so that the synthetic polypeptide adopts a functionally different structure relative to the structure of the parent polypeptide. It is also preferable that the size of the segments is large enough to minimise loss of T cell epitopes. In an especially preferred embodiment, the size of the segment is about 30 amino acids.

An optional spacer may be utilised to space adjacent segments relative to each other. Accordingly, an optional spacer may be interposed between some or all of the segments. The spacer suitably alters proteolytic processing and/or presentation of adjacent segment(s). In a preferred embodiment of this type, the spacer promotes or otherwise enhances proteolytic processing and/or presentation of adjacent segment(s). Preferably, the spacer comprises at least one amino acid. The at least one amino acid is suitably a neutral amino acid. The neutral amino acid is preferably alanine. Alternatively, the at least one amino acid is cysteine.

In a preferred embodiment, segments are selected such that they have partial sequence identity or homology with one or more other segments. Suitably, at one or both ends of a respective segment there is comprised at least 4 contiguous amino acids, preferably at least 7 contiguous amino acids, more preferably at least 10 contiguous amino acids, more preferably at least 15 contiguous amino acids and even more preferably at least 20 contiguous amino acids that are identical to, or homologous with, an amino acid sequence contained within one or more other of said segments. Preferably, at the or each

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end of a respective segment there is comprised less than 500 contiguous amino acids, more preferably less than 200 contiguous amino acids, more preferably less than 100 contiguous amino acids, more preferably less than 50 contiguous amino acids, more preferably less than 40 contiguous amino acids, and even more preferably less than 30 contiguous amino acids that are identical to, or homologous with, an amino acid sequence contained within one or more other of said segments. Such sequence overlap (also referred to elsewhere in the specification as "overlapping fragments" or "overlapping segments") is preferable to ensure potential epitopes at segment boundaries are not lost and to ensure that epitopes at or near segment boundaries are processed efficiently if placed beside or near amino acids that inhibit processing. Preferably, the segment size is about twice the size of the overlap.

In a preferred embodiment, when segments have partial sequence homology therebetween, the homologous sequences suitably comprise conserved and/or non-conserved amino acid differences. Exemplary conservative substitutions are listed in the following table.

15 **TABLE B**

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Original Residue	Exemplary Substitutions
Ala	Ser
Arg	Lys
Asn	Gln, His
Asp	Glu
Cys	Ser
Gln	Asn
Glu	Asp
Gly	Pro
His	Asn, Gln
Ile ·	Leu, Val
Leu	Ile, Val

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Original Residue	Exemplary Substitutions
Lys	Arg, Gln, Glu
Met	Leu, Ile,
Phe	Met, Leu, Tyr
Ser	Thr
Thr	Ser
· Trp	Tyr
Tyr	Trp, Phe
Val	Ile, Leu

Conserved or non-conserved differences may correspond to polymorphisms in corresponding parent polypeptides. Polymorphic polypeptides are expressed by various pathogenic organisms and cancers. For example, the polymorphic polypeptides may be expressed by different viral strains or clades or by cancers in different individuals.

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Sequence overlap between respective segments is preferable to minimise destruction of any epitope sequences that may result from any shuffling or rearrangement of the segments relative to their existing order in the parent polypeptide. If overlapping segments as described above are employed to form a synthetic polypeptide, it may not be necessary to change the order in which those segments are linked together relative to the order in which corresponding segments are normally present in the parent polypeptide. In this regard, such overlapping segments when linked together in the synthetic polypeptide can adopt a different structure relative to the structure of the parent polypeptide, wherein the different structure does not provide for one or more functions associated with the parent polypeptide. For example, in the case of four segments A-B-C-D each spanning 30 contiguous amino acids of the parent polypeptide and having a 10-amino acid overlapping sequence with one or more adjacent segments, the synthetic polypeptide will have duplicated 10-amino acid sequences bridging segments A-B, B-C and C-D. The presence of these duplicated sequences may be sufficient to render a different structure and to abrogate or alter function relative to the parent polypeptide.

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In a preferred embodiment, segment size is about 30 amino acids and sequence overlap at one or both ends of a respective segment is about 15 amino acids. However, it will be understood that other suitable segment sizes and sequence overlap sizes are contemplated by the present invention, which can be readily ascertained by persons of skill in the art.

It is preferable but not necessary to utilise all the segments of the parent polypeptide in the construction of the synthetic polypeptide. Suitably, at least 30%, preferably at least 40%, more preferably at least 50%, even more preferably at least 60%, even more preferably at least 70%, even more preferably at least 80% and still even more preferably at least 90% of the parent polypeptide sequence is used in the construction of the synthetic polypeptide. However, it will be understood that the more sequence information from a parent polypeptide that is utilised to construct the synthetic polypeptide, the greater the population coverage will be of the synthetic polypeptide as an immunogen. Preferably, no sequence information from the parent polypeptide is excluded (e.g., because of an apparent lack of immunological epitopes).

Persons of skill in the art will appreciate that when preparing a synthetic polypeptide against a pathogenic organism (e.g., a virus) or a cancer, it may be preferable to use sequence information from a plurality of different polypeptides expressed by the organism or the cancer. Accordingly, in a preferred embodiment, segments from a plurality of different polypeptides are linked together to form a synthetic polypeptide according to the invention. It is preferable in this respect to utilise as many parent polypeptides as possible from, or in relation to, a particular source in the construction of the synthetic polypeptide. The source of parent polypeptides includes, but is not limited to, a pathogenic organism and a cancer. Suitably, at least about 30%, preferably at least 40%, more preferably at least 50%, even more preferably at least 60%, even more preferably at least 70%, even more preferably at least 80% and still even more preferably at least 90% of the parent polypeptides expressed by the source is used in the construction of the synthetic polypeptide. Preferably, parent polypeptides from a virus include, but are not restricted to, latent polypeptides, regulatory polypeptides or polypeptides expressed early during their replication cycle. Suitably, parent polypeptides from a parasite or bacterium include, but are not restricted to, secretory polypeptides and polypeptides expressed on the surface of

the parasite or bacteria. It is preferred that parent polypeptides from a cancer or tumour are cancer specific polypeptides.

Suitably, hypervariable sequences within the parent polypeptide are excluded from the construction of the synthetic polypeptide.

The synthetic polypeptides of the inventions may be prepared by any suitable procedure known to those of skill in the art. For example, the polypeptide may be synthesised using solution synthesis or solid phase synthesis as described, for example, in Chapter 9 of Atherton and Shephard (1989, Solid Phase Peptide Synthesis: A Practical Approach. IRL Press, Oxford) and in Roberge et al (1995, Science 269: 202). Syntheses may employ, for example, either *t*-butyloxycarbonyl (t-Boc) 9or fluorenylmethyloxycarbonyl (Fmoc) chemistries (see Chapter 9.1, of Coligan et al., CURRENT PROTOCOLS IN PROTEIN SCIENCE, John Wiley & Sons, Inc. 1995-1997: Stewart and Young, 1984, Solid Phase Peptide Synthesis, 2nd ed. Pierce Chemical Co., Rockford, Ill; and Atherton and Shephard, supra).

Alternatively, the polypeptides may be prepared by a procedure including the steps of:

- (a) preparing a synthetic construct including a synthetic polynucleotide encoding a synthetic polypeptide wherein said synthetic polynucleotide is operably linked to a regulatory polynucleotide, wherein said synthetic polypeptide comprises a plurality of different segments of a parent polypeptide, wherein said segments are linked together in a different relationship relative to their linkage in the parent polypeptide;
 - (b) introducing the synthetic construct into a suitable host cell;
- (c) culturing the host cell to express the synthetic polypeptide from said synthetic construct; and
- (d) isolating the synthetic polypeptide.

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The synthetic construct is preferably in the form of an expression vector. For example, the expression vector can be a self-replicating extra-chromosomal vector such as a plasmid, or a vector that integrates into a host genome. Typically, the regulatory polynucleotide may include, but is not limited to, promoter sequences, leader or signal

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sequences, ribosomal binding sites, transcriptional start and stop sequences, translational start and termination sequences, and enhancer or activator sequences. Constitutive or inducible promoters as known in the art are contemplated by the invention. The promoters may be either naturally occurring promoters, or hybrid promoters that combine elements of more than one promoter. The regulatory polynucleotide will generally be appropriate for the host cell used for expression. Numerous types of appropriate expression vectors and suitable regulatory polynucleotides are known in the art for a variety of host cells.

In a preferred embodiment, the expression vector contains a selectable marker gene to allow the selection of transformed host cells. Selection genes are well known in the art and will vary with the host cell used.

The expression vector may also include a fusion partner (typically provided by the expression vector) so that the synthetic polypeptide of the invention is expressed as a fusion polypeptide with said fusion partner. The main advantage of fusion partners is that they assist identification and/or purification of said fusion polypeptide. In order to express said fusion polypeptide, it is necessary to ligate a polynucleotide according to the invention into the expression vector so that the translational reading frames of the fusion partner and the polynucleotide coincide.

Well known examples of fusion partners include, but are not limited to, glutathione-S-transferase (GST), Fc portion of human IgG, maltose binding protein (MBP) and hexahistidine (HIS₆), which are particularly useful for isolation of the fusion polypeptide by affinity chromatography. For the purposes of fusion polypeptide purification by affinity chromatography, relevant matrices for affinity chromatography are glutathione-, amylose-, and nickel- or cobalt-conjugated resins respectively. Many such matrices are available in "kit" form, such as the QIAexpressTM system (Qiagen) useful with (HIS₆) fusion partners and the Pharmacia GST purification system. In a preferred embodiment, the recombinant polynucleotide is expressed in the commercial vector pFLAGTM.

Another fusion partner well known in the art is green fluorescent protein (GFP). This fusion partner serves as a fluorescent "tag" which allows the fusion polypeptide of the invention to be identified by fluorescence microscopy or by flow cytometry. The GFP tag is useful when assessing subcellular localisation of a fusion polypeptide of the invention,

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or for isolating cells which express a fusion polypeptide of the invention. Flow cytometric methods such as fluorescence activated cell sorting (FACS) are particularly useful in this latter application. Preferably, the fusion partners also have protease cleavage sites, such as for Factor X_a , Thrombin and inteins (protein introns), which allow the relevant protease to partially digest the fusion polypeptide of the invention and thereby liberate the recombinant polypeptide of the invention therefrom. The liberated polypeptide can then be isolated from the fusion partner by subsequent chromatographic separation. Fusion partners according to the invention also include within their scope "epitope tags", which are usually short peptide sequences for which a specific antibody is available. Well known examples of epitope tags for which specific monoclonal antibodies are readily available include c-Myc, influenza virus, haemagglutinin and FLAG tags. Alternatively, a fusion partner may be provided to promote other forms of immunity. For example, the fusion partner may be an antigen-binding molecule that is immuno-interactive with a conformational epitope on a target antigen or to a post-translational modification of a target antigen (e.g., an antigen-binding molecule that is immuno-interactive with a glycosylated target antigen).

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The step of introducing the synthetic construct into the host cell may be effected by any suitable method including transfection, and transformation, the choice of which will be dependent on the host cell employed. Such methods are well known to those of skill in the art.

Synthetic polypeptides of the invention may be produced by culturing a host cell transformed with the synthetic construct. The conditions appropriate for protein expression will vary with the choice of expression vector and the host cell. This is easily ascertained by one skilled in the art through routine experimentation.

Suitable host cells for expression may be prokaryotic or eukaryotic. One preferred host cell for expression of a polypeptide according to the invention is a bacterium. The bacterium used may be *Escherichia coli*. Alternatively, the host cell may be an insect cell such as, for example, *SF9* cells that may be utilised with a baculovirus expression system.

The synthetic polypeptide may be conveniently prepared by a person skilled in the art using standard protocols as for example described in Sambrook, *et al.*, MOLECULAR CLONING. A LABORATORY MANUAL (Cold Spring Harbor Press, 1989), in particular

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Sections 16 and 17; Ausubel *et al.*, CURRENT PROTOCOLS IN MOLECULAR BIOLOGY (John Wiley & Sons, Inc. 1994-1998), in particular Chapters 10 and 16; and Coligan *et al.*, CURRENT PROTOCOLS IN PROTEIN SCIENCE (John Wiley & Sons, Inc. 1995-1997), in particular Chapters 1, 5 and 6.

The amino acids of the synthetic polypeptide can be any non-naturally occurring or any naturally occurring amino acid. Examples of unnatural amino acids and derivatives during peptide synthesis include but are not limited to, use of 4-amino butyric acid, 6-aminohexanoic acid, 4-amino-3-hydroxy-5-phenylpentanoic acid, 4-amino-3-hydroxy-6-methylheptanoic acid, t-butylglycine, norleucine, norvaline, phenylglycine, ornithine, sarcosine, 2-thienyl alanine and/or D-isomers of amino acids. A list of unnatural amino acids contemplated by the present invention is shown in TABLE C.

TABLE C

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Non-conventional amino acid	Non-conventional amino acid
α-aminobutyric acid	L-N-methylalanine
α-amino-α-methylbutyrate	L-N-methylarginine
aminocyclopropane-carboxylate	L-N-methylasparagine
aminoisobutyric acid	L-N-methylaspartic acid
aminonorbornyl-carboxylate	L-N-methylcysteine
cyclohexylalanine	L-N-methylglutamine
cyclopentylalanine	L-N-methylglutamic acid
L-N-methylisoleucine	L-N-methylhistidine
D-alanine	L-N-methylleucine
D-arginine	L-N-methyllysine
D-aspartic acid	L-N-methylmethionine
D-cysteine	L-N-methylnorleucine
D-glutamate	L-N-methylnorvaline
D-glutamic acid	L-N-methylornithine

Non-conventional amino acid	Non-conventional amino acid
D-histidine	L-N-methylphenylalanine
D-isoleucine	L-N-methylproline
D-leucine	L-N-medlylserine
D-lysine	L-N-methylthreonine
D-methionine	L-N-methyltryptophan
D-ornithine	L-N-methyltyrosine
D-phenylalanine	L-N-methylvaline
D-proline	L-N-methylethylglycine
D-serine	L-N-methyl-t-butylglycine
D-threonine	L-norleucine
D-tryptophan	L-norvaline
D-tyrosine	α-methyl-aminoisobutyrate
D-valine	$lpha$ -methyl- γ -aminobutyrate
D-α-methylalanine	α-methylcyclohexylalanine
D-α-methylarginine	α-methylcylcopentylalanine
D- $lpha$ -methylasparagine	α -methyl- α -napthylalanine
D- $lpha$ -methylaspartate	α-methylpenicillamine
D- $lpha$ -methylcysteine	N-(4-aminobutyl)glycine
D-α-methylglutamine	N-(2-aminoethyl)glycine
D- $lpha$ -methylhistidine	N-(3-aminopropyl)glycine
D- α -methylisoleucine	N-amino-α-methylbutyrate
D-α-methylleucine	α-napthylalanine
D-α-methyllysine	N-benzylglycine
D-α-methylmethionine	N-(2-carbamylediyl)glycine
D-α-methylornithiine	N-(carbamylmethyl)glycine

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Non-conventional amino acid	Non-conventional amino acid
D-α-methylphenylalanine	N-(2-carboxyethyl)glycine
D-α-methylproline	N-(carboxymethyl)glycine
D-α-methylserine	N-cyclobutylglycine
D-α-methylthreonine	N-cycloheptylglycine
D-α-methyltryptophan	N-cyclohexylglycine
D-α-methyltyrosine	N-cyclodecylglycine
L-α-methylleucine	L-α-methyllysine
L- α -methylmethionine	L-α-methylnorleucine
L-α-methylnorvatine	L- $lpha$ -methylornithine
L-α-methylphenylalanine	L- $lpha$ -methylproline
L-α-methylserine	L- $lpha$ -methylthreonine
L-α-methyltryptophan	L-α-methyltyrosine
L-α-methylvaline	L-N-methylhomophenylalanine
N-(N-(2,2-diphenylethyl carbamylmethyl)glycine	N-(N-(3,3-diphenylpropyl carbamylmethyl)glycine
1-carboxy-1-(2,2-diphenyl-ethyl amino)cyclopropane	

The invention also contemplates modifying the synthetic polypeptides of the invention using ordinary molecular biological techniques so as to alter their resistance to proteolytic degradation or to optimise solubility properties or to render them more suitable as an immunogenic agent.

3. Preparation of synthetic polynucleotides of the invention

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The invention contemplates synthetic polynucleotides encoding the synthetic polypeptides as for example described in Section 2 *supra*. Polynucleotides encoding segments of a parent polypeptide can be produced by any suitable technique. For example, such polynucleotides can be synthesised *de novo* using readily available machinery.

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Sequential synthesis of DNA is described, for example, in U.S. Patent No 4,293,652. Instead of *de novo* synthesis, recombinant techniques may be employed including use of restriction endonucleases to cleave a polynucleotide encoding at least a segment of the parent polypeptide and use of ligases to ligate together in frame a plurality of cleaved polynucleotides encoding different segments of the parent polypeptide. Suitable recombinant techniques are described for example in the relevant sections of Ausubel, *et al.* (*supra*) and of Sambrook, *et al.*, (*supra*) which are incorporated herein by reference. Preferably, the synthetic polynucleotide is constructed using splicing by overlapping extension (SOEing) as for example described by Horton *et al.* (1990, *Biotechniques* 8(5): 528-535; 1995, *Mol Biotechnol.* 3(2): 93-99; and 1997, *Methods Mol Biol.* 67: 141-149). However, it should be noted that the present invention is not dependent on, and not directed to, any one particular technique for constructing the synthetic construct.

Various modifications to the synthetic polynucleotides may be introduced as a means of increasing intracellular stability and half-life. Possible modifications include but are not limited to the addition of flanking sequences of ribo- or deoxy- nucleotides to the 5' and/or 3' ends of the molecule or the use of phosphorothioate or 2' O-methyl rather than phosphodiesterase linkages within the oligodeoxyribonucleotide backbone.

The invention therefore contemplates a method of producing a synthetic polynucleotide as broadly described above, comprising linking together in the same reading frame at least two nucleic acid sequences encoding different segments of a parent polypeptide to form a synthetic polynucleotide, which encodes a synthetic polypeptide according to the invention. Suitably, nucleic acid sequences encoding at least 10 segments, preferably at least 20 segments, more preferably at least 40 segments and more preferably at least 100 segments of a parent polypeptide are employed to produce the synthetic polynucleotide.

Preferably, the method further comprises selecting segments of the parent polypeptide, reverse translating the selected segments and preparing nucleic acid sequences encoding the selected segments. It is preferred that the method further comprises randomly linking the nucleic acid sequences together to form the synthetic polynucleotide. The nucleic acid sequences may be oligonucleotides or polynucleotides.

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Suitably, segments are selected on the basis of size. Additionally, or in the alternative, segments are selected such that they have partial sequence identity or homology (i.e., sequence overlap) with one or more other segments. A number of factors can influence segment size and sequence overlap as mentioned above. In the case of sequence overlap, large amounts of duplicated nucleic acid sequences can sometimes result in sections of nucleic acid being lost during nucleic acid amplification (e.g., polymerase chain reaction, PCR) of such sequences, recombinant plasmid propagation in a bacterial host or during amplification of recombinant viruses containing such sequences. Accordingly, in a preferred embodiment, nucleic acid sequences encoding segments having sequence identity or homology with one or more other encoded segments are not linked together in an arrangement in which the identical or homologous sequences are contiguous. Also, it is preferable that different codons are used to encode a specific amino acid in a duplicated region. In this context, an amino acid of a parent polypeptide sequence is preferably reverse translated to provide a codon which, in the context of adjacent or local sequence elements, has a lower propensity of forming an undesirable sequence (e.g., a duplicated sequence or a palindromic sequence) that is refractory to the execution of a task (e.g., cloning or sequencing). Alternatively, segments may be selected such that they contain a carboxyl terminal leucine residue or such that reverse translated sequences encoding the segments contain restriction enzyme sites for convenient splicing of the reverse translated sequences.

The method optionally further comprises linking a spacer oligonucleotide encoding at least one spacer residue between segment-encoding nucleic acids. Such spacer residue(s) may be advantageous in ensuring that epitopes within the segments are processed and presented efficiently. Preferably, the spacer oligonucleotide encodes 2 to 3 spacer residues. The spacer residue is suitably a neutral amino acid, which is preferably alanine.

Optionally, the method further comprises linking in the same reading frame as other segment-containing nucleic acid sequences at least one variant nucleic acid sequence which encodes a variant segment having a homologous but not identical amino acid sequence relative to other encoded segments. Suitably, the variant segment comprises conserved and/or non-conserved amino acid differences relative to one or more other encoded segments. Such differences may correspond to polymorphisms as discussed

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above. In a preferred embodiment, degenerate bases are designed or built in to the at least one variant nucleic acid sequence to give rise to all desired homologous sequences.

When a large number of polymorphisms is intended to be covered, it is preferred that multiple synthetic polynucleotides are constructed rather than a single synthetic polynucleotide, which encodes all variant segments. For example, if there is less than 85% homology between polymorphic polypeptides, then it is preferred that more than one synthetic polynucleotide is constructed.

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Preferably, the method further comprises optimising the codon composition of the synthetic polynucleotide such that it is translated efficiently by a host cell. In this regard, it is well known that the translational efficiency of different codons varies between organisms and that such differences in codon usage can be utilised to enhance the level of protein expression in a particular organism. In this regard, reference may be made to Seed et al. (International Application Publication No WO 96/09378) who disclose the replacement of existing codons in a parent polynucleotide with synonymous codons to enhance expression of viral polypeptides in mammalian host cells. Preferably, the first or second most frequently used codons are employed for codon optimisation.

Preferably, gene splicing by overlap extension or "gene SOEing" (supra) is employed for the construction of the synthetic polynucleotide which is a PCR-based method of recombining DNA sequences without reliance on restriction sites and of directly generating mutated DNA fragments in vitro. By modifying the sequences incorporated into the 5'-ends of the primers, any pair of PCR products can be made to share a common sequence at one end. Under PCR conditions, the common sequence allows strands from two different fragments to hybridise to one another, forming an overlap. Extension of this overlap by DNA polymerase yields a recombinant molecule. However, a problem with long synthetic constructs is that mutations generally incorporate into amplified products during synthesis. In this instance, it is preferred that resolvase treatment is employed at various steps of the synthesis. Resolvases are bacteriophage-encoded endonucleases which recognise disruptions or mispairing of double stranded DNA and are primarily used by bacteriophages to resolve Holliday junctions (Mizuuchi, 1982; Youil et al., 1995). For example, T7 endonuclease I can be employed in synthetic DNA constructions to recognise mutations and cleave corrupted dsDNA. The mutated DNA strands are then hybridised to

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non-mutant or correct DNA sequences, which results in a mispairing of DNA bases. The mispaired bases are recognised by the resolvase, which then cleaves the DNA nearby leaving only correctly hybridised sequences intact. Preferably a thermostable resolvase enzyme is employed during splicing or amplification so that errors are not incorporated in downstream synthesis products.

Synthetic polynucleotides according to the invention can be operably linked to a regulatory polynucleotide in the form a synthetic construct as for example described in Section 2 *supra*. Synthetic constructs of the invention have utility *inter alia* as nucleic acid vaccines. The choice of regulatory polynucleotide and synthetic construct will depend on the intended host.

Exemplary expression vectors for expression of a synthetic polypeptide according to the invention include, but are not restricted to, modified Ankara Vaccinia virus as for example described by Allen *et al.* (2000, *J. Immunol.* 164(9): 4968-4978), fowlpox virus as for example described by Boyle and Coupar (1988, *Virus Res.* 10: 343-356) and the herpes simplex amplicons described for example by Fong *et al.* in U.S. Patent No. 6,051,428. Alternatively, Adenovirus and Epstein-Barr virus vectors, which are preferably capable of accepting large amounts of DNA or RNA sequence information, can be used.

Preferred promoter sequences that can be utilised for expression of synthetic polypeptides include the P7.5 or PE/L promoters as for example disclosed by Kumar and Boyle. (1990, *Virology* **179**: 151-158), CMV and RSV promoters.

The synthetic construct optionally further includes a nucleic acid sequence encoding an immunostimulatory molecule. The immunostimulatory molecule may be fusion partner of the synthetic polypeptide. Alternatively, the immunostimulatory molecule may be translated separately from the synthetic polypeptide. Preferably, the immunostimulatory molecule comprises a general immunostimulatory peptide sequence. For example, the immunostimulatory peptide sequence may comprise a domain of an invasin protein (Inv) from the bacteria *Yersinia* spp as for example disclosed by Brett *et al.* (1993, *Eur. J. Immunol.* 23: 1608-1614). This immune stimulatory property results from the capability of this invasin domain to interact with the β 1 integrin molecules present on T cells, particularly activated immune or memory T cells. A preferred embodiment of the invasin domain (Inv) for linkage to a synthetic polypeptide has been previously described

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in U.S. Pat. No. 5,759,551. The said Inv domain has the sequence: Thr-Ala-Lys-Ser-Lys-Lys-Phe-Pro-Ser-Tyr-Thr-Ala-Thr-Tyr-Gln-Phe [SEQ ID NO; 1467] or is an immune stimulatory homologue thereof from the corresponding region in another Yersinia species invasin protein. Such homologues thus may contain substitutions, deletions or insertions of amino acid residues to accommodate strain to strain variation, provided that the homologues retain immune stimulatory properties. The general immunostimulatory sequence may optionally be linked to the synthetic polypeptide by a spacer sequence.

In an alternate embodiment, the immunostimulatory molecule may comprise an immunostimulatory membrane or soluble molecule, which is suitably a T cell costimulatory molecule. Preferably, the T cell costimulatory molecule is a B7 molecule or a biologically active fragment thereof, or a variant or derivative of these. The B7 molecule includes, but is not restricted to, B7-1 and B7-2. Preferably, the B7 molecule is B7-1. Alternatively, the T cell costimulatory molecule may be an ICAM molecule such as ICAM-1 and ICAM-2.

In another embodiment, the immunostimulatory molecule can be a cytokine, which includes, but is not restricted to, an interleukin, a lymphokine, tumour necrosis factor and an interferon. Alternatively, the immunostimulatory molecule may comprise an immunomodulatory oligonucleotide as for example disclosed by Krieg in U.S. Patent No. 6,008,200.

Suitably, the size of the synthetic polynucleotide does not exceed the ability of host cells to transcribe, translate or proteolytically process and present epitopes to the immune system. Practitioners in the art will also recognise that the size of the synthetic polynucleotide can impact on the capacity of an expression vector to express the synthetic polynucleotide in a host cell. In this connection, it is known that the efficacy of DNA vaccination reduces with expression vectors greater that 20-kb. In such situations it is preferred that a larger number of smaller synthetic constructs is utilised rather than a single large synthetic construct.

4. Immunopotentiating compositions

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The invention also contemplates a composition, comprising an immunopotentiating agent selected from the group consisting of a synthetic polypeptide as

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described in Section 2, and a synthetic polynucleotide or a synthetic construct as described in Section 3, together with a pharmaceutically acceptable carrier. One or more immunopotentiating agents can be used as actives in the preparation immunopotentiating compositions. Such preparation uses routine methods known to persons skilled in the art. Typically, such compositions are prepared as injectables, either as liquid solutions or suspensions; solid forms suitable for solution in, or suspension in, liquid prior to injection may also be prepared. The preparation may also be emulsified. The active immunogenic ingredients are often mixed with excipients that are pharmaceutically acceptable and compatible with the active ingredient. Suitable excipients are, for example, water, saline, dextrose, glycerol, ethanol, or the like and combinations thereof. In addition, if desired, the vaccine may contain minor amounts of auxiliary substances such as wetting or emulsifying agents, pH buffering agents, and/or adjuvants that enhance the effectiveness of the vaccine. Examples of adjuvants which may be effective include but are not limited to: aluminium hydroxide, N-acetyl-muramyl-L-threonyl-D-isoglutamine (thur-MDP), Nacetyl-nor-muramyl-L-alanyl-D-isoglutamine (CGP 11637, referred to as nor-MDP), Nacetylmuramyl-L-alanyl-D-isoglutaminyl-L-alanine-2-(1'-2'-dipalmitoyl-sn-glycero-3hydroxyphosphoryloxy)-ethylamine (CGP 1983A, referred to as MTP-PE), and RIBI, which contains three components extracted from bacteria, monophosphoryl lipid A, trehalose dimycolate and cell wall skeleton (MPL+TDM+CWS) in a 2% squalene/Tween 80 emulsion. For example, the effectiveness of an adjuvant may be determined by measuring the amount of antibodies resulting from the administration of the composition, wherein those antibodies are directed against one or more antigens presented by the treated cells of the composition.

The immunopotentiating agents may be formulated into a composition as neutral or salt forms. Pharmaceutically acceptable salts include the acid addition salts (formed with free amino groups of the peptide) and which are formed with inorganic acids such as, for example, hydrochloric or phosphoric acids, or such organic acids such as acetic, oxalic, tartaric, maleic, and the like. Salts formed with the free carboxyl groups may also be derived from inorganic basis such as, for example, sodium, potassium, ammonium, calcium, or ferric hydroxides, and such organic basis as isopropylamine, trimethylamine, 2-ethylamino ethanol, histidine, procaine, and the like.

If desired, devices or compositions containing the immunopotentiating agents suitable for sustained or intermittent release could be, in effect, implanted in the body or topically applied thereto for the relatively slow release of such materials into the body.

The compositions are conventionally administered parenterally, by injection, for example, either subcutaneously or intramuscularly. Additional formulations which are suitable for other modes of administration includes suppositories and, in some cases, oral formulations. For suppositories, traditional binders and carriers may include, for example, polyalkylene glycols or triglycerides; such suppositories may be formed from mixtures containing the active ingredient in the range of 0.5% to 10%, preferably 1%-2%. Oral formulations include such normally employed excipients as, for example, pharmaceutical grades of mannitol, lactose, starch, magnesium carbonate, and the like. These compositions take the form of solutions, suspensions, tablets, pills, capsules, sustained release formulations or powders and contain 10%-95% of active ingredient, preferably 25%-70%.

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Administration of the gene therapy construct to said mammal, preferably a human, may include delivery via direct oral intake, systemic injection, or delivery to selected tissue(s) or cells, or indirectly via delivery to cells isolated from the mammal or a compatible donor. An example of the latter approach would be stem cell therapy, wherein isolated stem cells having potential for growth and differentiation are transfected with the vector comprising the Sox18 nucleic acid. The stem cells are cultured for a period and then transferred to the mammal being treated.

With regard to nucleic acid based compositions, all modes of delivery of such compositions are contemplated by the present invention. Delivery of these compositions to cells or tissues of an animal may be facilitated by microprojectile bombardment, liposome mediated transfection (e.g., lipofectin or lipofectamine), electroporation, calcium phosphate or DEAE-dextran-mediated transfection, for example. In an alternate embodiment, a synthetic construct may be used as a therapeutic or prophylactic composition in the form of a "naked DNA" composition as is known in the art. A discussion of suitable delivery methods may be found in Chapter 9 of CURRENT PROTOCOLS IN MOLECULAR BIOLOGY (Eds. Ausubel et al.; John Wiley & Sons Inc., 1997 Edition) or on the Internet site DNAvaccine.com. The compositions may be administered by intradermal (e.g., using panjetTM delivery) or intramuscular routes.

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The step of introducing the synthetic polynucleotide into a target cell will differ depending on the intended use and species, and can involve one or more of non-viral and viral vectors, cationic liposomes, retroviruses, and adenoviruses such as, for example, described in Mulligan, R.C., (1993 *Science* 260 926-932) which is hereby incorporated by reference. Such methods can include, for example:

- A. Local application of the synthetic polynucleotide by injection (Wolff et al., 1990, Science 247 1465-1468, which is hereby incorporated by reference), surgical implantation, instillation or any other means. This method can also be used in combination with local application by injection, surgical implantation, instillation or any other means, of cells responsive to the protein encoded by the synthetic polynucleotide so as to increase the effectiveness of that treatment. This method can also be used in combination with local application by injection, surgical implantation, instillation or any other means, of another factor or factors required for the activity of said protein.
- B. General systemic delivery by injection of DNA, (Calabretta et al., 1993, Cancer Treat. Rev. 19 169-179, which is incorporated herein by reference), or RNA, alone or in combination with liposomes (Zhu et al., 1993, Science 261 209-212, which is incorporated herein by reference), viral capsids or nanoparticles (Bertling et al., 1991, Biotech. Appl. Biochem. 13 390-405, which is incorporated herein by reference) or any other mediator of delivery. Improved targeting might be achieved by linking the synthetic polynucleotide to a targeting molecule (the so-called "magic bullet" approach employing, for example, an antibody), or by local application by injection, surgical implantation or any other means, of another factor or factors required for the activity of the protein encoding said synthetic polynucleotide, or of cells responsive to said protein.
 - C. Injection or implantation or delivery by any means, of cells that have been modified ex vivo by transfection (for example, in the presence of calcium phosphate: Chen et al., 1987, Mole. Cell Biochem. 7 2745-2752, or of cationic lipids and polyamines: Rose et al., 1991, BioTech. 10 520-525, which articles are incorporated herein by reference), infection, injection, electroporation (Shigekawa et al., 1988, BioTech. 6 742-751, which is incorporated herein by reference) or any other way so as to increase the

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expression of said synthetic polynucleotide in those cells. The modification can be mediated by plasmid, bacteriophage, cosmid, viral (such as adenoviral or retroviral; Mulligan, 1993, Science 260 926-932; Miller, 1992, Nature 357 455-460; Salmons et al., 1993, Hum. Gen. Ther. 4 129-141, which articles are incorporated herein by reference) or other vectors, or other agents of modification such as liposomes (Zhu et al., 1993, Science 261 209-212, which is incorporated herein by reference), viral capsids or nanoparticles (Bertling et al., 1991, Biotech. Appl. Biochem. 13 390-405, which is incorporated herein by reference), or any other mediator of modification. The use of cells as a delivery vehicle for genes or gene products has been described by Barr et al., 1991, Science 254 1507-1512 and by Dhawan et al., 1991, Science 254 1509-1512, which articles are incorporated herein by reference. Treated cells can be delivered in combination with any nutrient, growth factor, matrix or other agent that will promote their survival in the treated subject.

Also encapsulated by the present invention is a method for treatment and/or prophylaxis of a disease or condition, comprising administering to a patient in need of such treatment a therapeutically effective amount of a composition as broadly described above. The disease or condition may be caused by a pathogenic organism or a cancer as for example described above.

In a preferred embodiment, the immunopotentiating composition of the invention is suitable for treatment of, or prophylaxis against, a cancer. Cancers which could be suitably treated in accordance with the practices of this invention include cancers of the lung, breast, ovary, cervix, colon, head and neck, pancreas, prostate, stomach, bladder, kidney, bone liver, oesophagus, brain, testicle, uterus, melanoma and the various leukemias and lymphomas.

In an alternate embodiment, the immunopotentiating composition is suitable for treatment of, or prophylaxis against, a viral, bacterial or parasitic infection. Viral infections contemplated by the present invention include, but are not restricted to, infections caused by HIV, Hepatitis, Influenza, Japanese encephalitis virus, Epstein-Barr virus and respiratory syncytial virus. Bacterial infections include, but are not restricted to, those caused by Neisseria species, Meningococcal species, Haemophilus species Salmonella species, Streptococcal species, Legionella species and Mycobacterium species. Parasitic

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infections encompassed by the invention include, but are not restricted to, those caused by *Plasmodium* species, *Schistosoma* species, *Leishmania* species, *Trypanosoma* species, *Toxoplasma* species and *Giardia* species.

The above compositions or vaccines may be administered in a manner compatible with the dosage formulation, and in such amount as is therapeutically effective to alleviate patients from the disease or condition or as is prophylactically effective to prevent incidence of the disease or condition in the patient. The dose administered to a patient, in the context of the present invention, should be sufficient to effect a beneficial response in a patient over time such as a reduction or cessation of blood loss. The quantity of the composition or vaccine to be administered may depend on the subject to be treated inclusive of the age, sex, weight and general health condition thereof. In this regard, precise amounts of the composition or vaccine for administration will depend on the judgement of the practitioner. In determining the effective amount of the composition or vaccine to be administered in the treatment of a disease or condition, the physician may evaluate the progression of the disease or condition over time. In any event, those of skill in the art may readily determine suitable dosages of the composition or vaccine of the invention.

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In a preferred embodiment, DNA-based immunopotentiating agent (e.g., 100 μ g) is delivered intradermally into a patient at day 1 and at week 8 to prime the patient. A recombinant poxvirus (e.g., at 10^7 pfu/mL) from which substantially the same immunopotentiating agent can be expressed is then delivered intradermally as a booster at weeks 16 and 24, respectively.

The effectiveness of the immunisation may be assessed using any suitable technique. For example, CTL lysis assays may be employed using stimulated splenocytes or peripheral blood mononuclear cells (PBMC) on peptide coated or recombinant virus infected cells using ⁵¹Cr labelled target cells. Such assays can be performed using for example primate, mouse or human cells (Allen *et al.*, 2000, *J. Immunol.* 164(9): 4968-4978 also Woodberry *et al.*, *infra*). Alternatively, the efficacy of the immunisation may be monitored using one or more techniques including, but not limited to, HLA class I Tetramer staining - of both fresh and stimulated PBMCs (see for example Allen *et al.*, *supra*), proliferation assays (Allen *et al.*, *supra*), ElispotTM Assays and intracellular INF-

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gamma staining (Allen *et al.*, *supra*), ELISA Assays - for linear B cell responses; and Western blots of cell sample expressing the synthetic polynucleotides.

5. Computer related embodiments

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The design or construction of a synthetic polypeptide sequence or a synthetic polynucleotide sequence according to the invention is suitably facilitated with the assistance of a computer programmed with software, which *inter alia* fragments a parent sequence into fragments, and which links those fragments together in a different relationship relative to their linkage in the parent sequence. The ready use of a parent sequence for the construction of a desired synthetic molecule according to the invention requires that it be stored in a computer-readable format. Thus, in accordance with the present invention, sequence data relating to a parent molecule (e.g., a parent polypeptide) is stored in a machine-readable storage medium, which is capable of processing the data to fragment the sequence of the parent molecule into fragments and to link together the fragments in a different relationship relative to their linkage in the parent molecule.

Therefore, another embodiment of the present invention provides a machine-readable data storage medium, comprising a data storage material encoded with machine readable data which, when used by a machine programmed with instructions for using said data, fragments a parent sequence into fragments, and links those fragments together in a different relationship relative to their linkage in the parent sequence. In a preferred embodiment of this type, a machine-readable data storage medium is provided that is capable of reverse translating the sequence of a respective fragment to provide a nucleic acid sequence encoding the fragment and to link together in the same reading frame each of the nucleic acid sequences to provide a polynucleotide sequence that codes for a polypeptide sequence in which said fragments are linked together in a different relationship relative to their linkage in a parent polypeptide sequence.

In another embodiment, the invention encompasses a computer for designing the sequence of a synthetic polypeptide and/or a synthetic polynucleotide of the invention, wherein the computer comprises wherein said computer comprises: (a) a machine readable data storage medium comprising a data storage material encoded with machine readable data, wherein said machine readable data comprises the sequence of a parent polypeptide; (b) a working memory for storing instructions for processing said machine-readable data;

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(c) a central-processing unit coupled to said working memory and to said machine-readable data storage medium, for processing said machine-readable data into said synthetic polypeptide sequence and/or said synthetic polynucleotide; and (d) an output hardware coupled to said central processing unit, for receiving said synthetic polypeptide sequence and/or said synthetic polynucleotide.

In yet another embodiment, the invention contemplates a computer program product for designing the sequence of a synthetic polynucleotide of the invention, comprising code that receives as input the sequence of a parent polypeptide, code that fragments the sequence of the parent polypeptide into fragments, code that reverse translates the sequence of a respective fragment to provide a nucleic acid sequence encoding the fragment, code that links together in the same reading frame each said nucleic acid sequence to provide a polynucleotide sequence that codes for a polypeptide sequence in which said fragments are linked together in a different relationship relative to their linkage in the parent polypeptide sequence, and a computer readable medium that stores the codes.

A version of these embodiments is presented in Figure 23, which shows a system 10 including a computer 11 comprising a central processing unit ("CPU") 20, a working memory 22 which may be, e.g., RAM (random-access memory) or "core" memory, mass storage memory 24 (such as one or more disk drives or CD-ROM drives), one or more cathode-ray tube ("CRT") display terminals 26, one or more keyboards 28, one or more input lines 30, and one or more output lines 40, all of which are interconnected by a conventional bidirectional system bus 50.

Input hardware 36, coupled to computer 11 by input lines 30, may be implemented in a variety of ways. For example, machine-readable data of this invention may be inputted via the use of a modem or modems 32 connected by a telephone line or dedicated data line 34. Alternatively or additionally, the input hardware 36 may comprise CD. Alternatively, ROM drives or disk drives 24 in conjunction with display terminal 26, keyboard 28 may also be used as an input device.

Output hardware 46, coupled to computer 11 by output lines 40, may similarly be implemented by conventional devices. By way of example, output hardware 46 may include CRT display terminal 26 for displaying a synthetic polynucleotide sequence or a synthetic polypeptide sequence as described herein. Output hardware might also include a

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printer 42, so that hard copy output may be produced, or a disk drive 24, to store system output for later use.

In operation, CPU 20 coordinates the use of the various input and output devices 36,46 coordinates data accesses from mass storage 24 and accesses to and from working memory 22, and determines the sequence of data processing steps. A number of programs may be used to process the machine readable data of this invention. Exemplary programs may use for example the steps outlined in the flow diagram illustrated in Figure 24. Broadly, these steps include (1) inputting at least one parent polypeptide sequence; (2) optionally adding to alanine spacers at the ends of each polypeptide sequence; (3) fragmenting the polypeptide sequences into fragments (e.g., 30 amino acids long), which are preferably overlapping (e.g., by 15 amino acids); (4) reverse translating the fragment to provide a nucleic acid sequence for each fragment and preferably using for the reverse translation first and second most translationally efficient codons for a cell type, wherein the codons are preferably alternated out of frame with each other in the overlaps of consecutive fragments; (5) randomly rearranging the fragments; (6) checking whether rearranged fragments recreate at least a portion of a parent polypeptide sequence; (7) repeating randomly rearranging the fragments when rearranged fragments recreate said at least a portion; or otherwise (8) linking the rearranged fragments together to produce a synthetic polypeptide sequence and/or a synthetic polynucleotide sequence; and (9) outputting said synthetic polypeptide sequence and/or a synthetic polynucleotide sequence. An example of an algorithm which uses inter alia the aforementioned steps is shown in Figure 25. By way of example, this algorithm has been used for the design of synthetic polynucleotides and synthetic polypeptides according to the present invention for Hepatitis C 1a and for melanoma, as illustrated in Figures 26 and 27.

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Figure 28 shows a cross section of a magnetic data storage medium 100 which can be encoded with machine readable data, or set of instructions, for designing a synthetic molecule of the invention, which can be carried out by a system such as system 10 of Figure 23. Medium 100 can be a conventional floppy diskette or hard disk, having a suitable substrate 101, which may be conventional, and a suitable coating 102, which may be conventional, on one or both sides, containing magnetic domains (not visible) whose polarity or orientation can be altered magnetically. Medium 100 may also have an opening (not shown) for receiving the spindle of a disk drive or other data storage device 24. The

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magnetic domains of coating 102 of medium 100 are polarised or oriented so as to encode in manner which may be conventional, machine readable data such as that described herein, for execution by a system such as system 10 of Figure 23.

Figure 29 shows a cross section of an optically readable data storage medium 110 which also can be encoded with such a machine-readable data, or set of instructions, for designing a synthetic molecule of the invention, which can be carried out by a system such as system 10 of Figure 23. Medium 110 can be a conventional compact disk read only memory (CD-ROM) or a rewritable medium such as a magneto-optical disk, which is optically readable and magneto-optically writable. Medium 100 preferably has a suitable substrate 111, which may be conventional, and a suitable coating 112, which may be conventional, usually of one side of substrate 111.

In the case of CD-ROM, as is well known, coating 112 is reflective and is impressed with a plurality of pits 113 to encode the machine-readable data. The arrangement of pits is read by reflecting laser light off the surface of coating 112. A protective coating 114, which preferably is substantially transparent, is provided on top of coating 112.

In the case of a magneto-optical disk, as is well known, coating 112 has no pits 113, but has a plurality of magnetic domains whose polarity or orientation can be changed magnetically when heated above a certain temperature, as by a laser (not shown). The orientation of the domains can be read by measuring the polarisation of laser light reflected from coating 112. The arrangement of the domains encodes the data as described above.

In order that the invention may be readily understood and put into practical effect, particular preferred non-limiting embodiments will now be described as follows.

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EXAMPLES

EXAMPLE 1

Preparation of an HIV Savine

Experimental Protocol

5 Plasmids

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The plasmid pDNAVacc is ampicillin resistant and contains an expression cassette comprising a CMV promoter and enhancer, a synthetic intron, a multiple cloning site (MCS) and a SV40poly A signal sequence (Thomson *et al.*, 1998). The plasmid pTK7.5 and contains a selection cassette, a pox virus 7.5 early/late promoter and a MCS flanked on either side by Vaccinia virus TK gene sequences.

Recombinant Vaccinia Viruses

Recombinant Vaccinia viruses expressing the gag, env (IIB) and pol (LAI) genes of HIV-1 were used as previously described and denoted VV-GAG, VV-POL, VV-ENV (Woodberry et al., 1999; Kent et al., 1998).

15 Marker Rescue Recombination

Recombinant Vaccinia viruses containing Savine constructs were generated by marker rescue recombination, using protocols described previously (Boyle *et al.*, 1985). Plaque purified viruses were tested for the TK phenotype and for the appropriate genome arrangement by Southern blot and PCR.

20 Oligonucleotides

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Oligonucleotides 50 nmol scale and desalted were purchased from Life Technologies. Short oligonucleotides were resuspended in 100 μ L of water, their concentration determined, then diluted to 20 μ M for use in PCR or sequencing reactions. Long oligonucleotides for splicing reactions were denatured for 5 minutes at 94°C in 20 μ L of formamide loading buffer then 0.5 μ L gel purified on a 6% polyacrylamide gel.

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Gel slices containing full-length oligonucleotides were visualised with ethidium bromide, excised, placed in EppendorfTM tubes, combined with 200 μ L of water before being crushed using the plunger of a 1 mL syringe. Before being used in splicing reactions the crushed gel was resuspended in an appropriate volume of buffer and 1-2 μ L of the resuspendate used directly in the splicing reactions.

Sequencing

Sequencing was performed using Dye terminator sequencing reactions and analyzed by the Biomedical Resource Facility at the John Curtin School of Medical Research using an ABI automated sequencer.

10 Restimulation of Lymphocytes from HIV Infected Patients

Two pools of recombinant Vaccinia viruses containing VV-AC1 + VV-BC1 (Pool 1) or VV-AC2 + VV-BC2 + VV-CC2 (Pool 2) were used to restimulate lymphocytes from the blood samples of HIV-infected patients. Briefly CTL lines were generated from HIV-infected donor PBMC. A fifth of the total PBMC were infected with either Pool 1 or Pool 2 Vaccinia viruses then added back to the original cell suspension. The infected cell suspension was then cultured with IL-7 for 1 week.

CTL Assays

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Restimulated PBMCs were used as effectors in a standard ⁵¹Cr-release CTL assay. Targets were autologous EBV-transformed lymphoblastoid cell lines (LCLs) infected with the following viruses: Pool 1, Pool 2,VV-GAG, VV-POL or VV-ENV. Assay controls included uninfected targets, targets infected with VV-lacZ (virus control) and K562 cells.

Results

HIV Savine Design

A main goal of the Savine strategy is to include as much protein sequence information from a pathogen or cancer as possible in such a way that potential T cell epitopes remain intact and so that the vaccine or therapy is extremely safe. An HIV Savine is described herein not only to compare this strategy to other strategies but also, to produce

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an HIV vaccine that would provide the maximum possible population coverage as well as catering for the major HIV clades.

A number of design criteria was first determined to exploit the many advantages of using a synthetic approach. One advantage is that it is possible to use consensus protein sequences to design these vaccines. Using consensus sequences for a highly variable virus like HIV should provide better vaccine coverage because individual viral isolate sequences may have lost epitopes which induce CTL against the majority of other viral isolates. Thus, using the consensus sequences of each HTV clade rather than individual isolate sequences should provide better vaccine coverage. Taking this one step further, a consensus sequence that covers all HIV clades should theoretically provide better coverage than using just the consensus sequences for individual clades. Before designing such a sequence however, it was decided that a more appropriate and focussed HIV vaccine might be constructed if the various clades were first ranked according to their relative importance. To establish such a ranking the following issues were considered, current prevalence of each clade, the rate at which each clade is increasing and the capacity of various regions of the world to cope with the HIV pandemic (Figures 1 and 2). These criteria produced the following ranking, Clade $E \ge \text{clade } A > \text{clade } C > \text{clade } B > \text{clade } D > \text{other clades.}$ Clades E and A were considered to almost equal since they are very similar except in their envelope protein sequences, which differ considerably.

Another advantage of synthesising a designed sequence is that it is possible to incorporate degenerate sequences into their design. In the case of HIV, this means that more than one amino acid can be included at various positions to improve the ability of the vaccine to cater for the various HIV clades and isolates. Coverage is improved because mutations in different HIV clades and also in individual isolate sequences, while mostly destroying specific T cell epitopes, can result in the formation of new potentially useful epitopes nearby (Goulder et al., 1997). Incorporating degenerate amino acid sequences, however, also means that more than one construct must be made and mixed together. The number of constructs required depends on the frequency with which mutations are incorporated into the design. While this approach requires the construction of additional constructs, these constructs can be prepared from the same set of degenerate long oligonucleotides, significantly reducing the cost of providing such considerable interclade coverage.

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A set of degeneracy rules was developed for the incorporation of amino acid mutations into the design which meant that a maximum of eight constructs would be required so that theoretically all combinations were present, as follows: 1) Two amino acids at three positions (or less) within any group of nine amino acids (*i.e.*, present in a CTL epitope); 2) Three amino acids at one position and two at another (or not) within any group of nine amino acids; 3) Four amino acids at one position and two at another (or not) within any group of nine amino acids. The reason why these rules were applied to nine amino acids (the average CTL epitope size) and not to larger stretches of amino acid sequence to cater for class II restricted epitopes, is because class II-restricted epitopes generally have a core sequence of nine amino acids in the middle which bind specifically to class II MHC molecules with the extra flanking sequences stabilising binding, by associating with either side of class II MHC antigens in a largely sequence independent manner (Brown *et al.*, 1993).

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Using the HIV clade ranking described above, the amino acid degeneracy rules and in some situations the similarity between amino acids, a degenerate consensus protein sequence was designed for each HIV protein using the consensus protein sequences for each HIV clade compiled by the Los Alamos HIV sequence database (Figures 3-11) (HIV Molecular Immunology Database, 1997). It is important to note that in some situations the order with which each of the above design criteria was applied was altered. Each time this was done the primary goal however was to increase the ability of the Savine to cater for interclade differences. Two isolate sequences, GenBank accession U51189 and U46016, for clade E and clade C, respectively, were used when a consensus sequence for some HIV proteins from these two clades was unavailable (Gao *et al.*, 1996; Salminen *et al.*, 1996). The design of a consensus sequence for the hypervariable regions of the HIV envelope protein and in some cases between these regions (hypervariable regions 1-2 and 3-5) was difficult and so these regions were excluded from the vaccine design.

Once a degenerate consensus sequence was designed for each HIV protein, an approach was then determined for incorporating all the protein sequences safely into the vaccine. One convenient approach to ensure that a vaccine will be safe is to systematically fragment and randomly rearrange the protein sequences together thus abrogating or otherwise altering their structure and function. The protein sequences still have to be immunologically functional however, meaning that the process used to fragment the

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sequences should not destroy potential epitopes. To decide on the best approach for systematically fragmenting protein sequences, the main criteria used was the size of T epitopes and their processing requirements. Class I-restricted T cell epitopes are 8-10 amino acids long and generally require 2-3 natural flanking amino acids to ensure their efficient processing and presentation if placed next to unnatural flanking residues (Del Val et al., 1991; Thomson et al., 1995). Class II-restricted T cell epitopes range between 12-25 amino acids long and do appear to require natural flanking residues for processing however, it is difficult to rule out a role for natural flanking residues in all cases due to the complexity of their processing pathways (Thomson et al., 1998). Also class II-restricted epitopes despite being larger than CTL epitopes generally have a core sequence of 9-10 amino acids, which binds to MHC molecules in a sequence specific fashion. Thus, based on current knowledge, it was decided that an advantageous approach was to overlap the fragments by at least 15 amino acids to ensure that potential epitopes which might lie across fragment boundaries are not lost and to ensure that CTL epitopes near fragment boundaries, that are placed beside or near inhibitory amino acids in adjacent fragments, are processed efficiently. In deciding the optimal fragment size, the main criteria used were that size had to be small enough to cause the maximum disruption to the structure and function of proteins but large enough to cover the sequence information as efficiently as possible without any further unnecessary duplication. Based on these criteria the fragments would be twice the overlap size, in this case 30 amino acids long.

The designed degenerate protein sequences were then separated into fragments 30 amino acid long and overlapping by fifteen amino acids. Two alanine amino acids were also added to the start and end of the first and last fragment for each protein or envelop protein segment to ensure these fragments were not placed directly adjacent to amino acids capable of blocking epitope processing (Del Val et al., 1991). The next step was to reverse translate each protein sequence back into DNA. Duplicating DNA sequences was avoided when constructing DNA sequences encoding a tandem repeat of identical or homologous amino acid sequences to maximise expression of the Savine. In this regard, the first and second most commonly used mammalian codons (shown in Figure 12) were assigned to amino acids in these repeat regions, wherein a first codon was used to encode an amino acid in one of the repeated sequences and wherein a second but synonymous codon was used for the other repeated sequence (e.g., see the gag HIV protein in Figure 13). To cater

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for the designed amino acid mutations more than one base was assigned to some positions using the IUPAC DNA codes without exceeding more than three base variations (eight possible combinations) in any group of 27 bases (Figure 12). Where a particular combination of amino acids could not be incorporated, because too many degenerate bases would be required, some or all of the amino acid degeneracy was removed according to the protein consensus design rules outlined above. Also the degenerate codons were checked to determine if they could encode a stop codon, if stop codons could not be avoided then the amino acid degeneracy was also simplified again according to the protein consensus design rules outlined above.

The designed DNA segments were then scrambled randomly and joined to create twenty-two subcassettes approximately 840 bp in size. Extra DNA sequences incorporating sites for one of the cohesive restriction enzymes *XbaI*, *SpeI*, *AvrII* or *NheI* and 3 additional base pairs (to cater for premature Taq polymerase termination) were then added to each end of each subcassette (Figure 14). Some of these extra DNA sequences also contained, the cohesive restriction sites for *SalI* or *XhoI*, Kozak signal sequences and start or stop codons to enable the subcassettes to be joined and expressed either as three large cassettes or one full length protein (Figures 14 and 15).

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In designing the HIV Savine one issue that required investigation was whether such a large DNA molecule would be fully expressed and whether epitopes encoded near the end of the molecule would be efficiently presented to the immune system. The inventors also wished to show that mixing two or more degenerate Savine constructs together could induce T cell responses that recognise mutated sequences. To examine both issues DNA coding for a degenerate murine influenza nucleoprotein CTL epitope, NP365-373, which differs by two amino acids at positions 71 and 72 in influenza strain A/PR/8/34 compared to the A/NT/60/68strain and restricted by H2-Db, was inserted before the last stop codon at the end of the HIV Savine design (Figure 15). An important and unusual characteristic of both of these naturally occurring NP365-373 sequences, which enabled the present inventors to examine the effectiveness of incorporating mutated sequences, is that they generate CTL responses which do not cross react with the alternate sequence (Townsend *et. al.*, 1986). This is an unusual characteristic because epitopes not destroyed by mutation usually induce CTL responses that cross-react.

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Up to ten long oligonucleotides up to 100 bases long and two short amplification oligonucleotides were synthesised to enable construction of each subcassette (Life Technologies). In designing each oligonucleotide the 3' end and in most cases also the 5' end had to be either a 'c' or a 'g' to ensure efficient extension during PCR splicing. The overlap region for each long oligonucleotide was designed to be at least 16 bp with approximately 50% G/C content. Also oligonucleotide overlaps were not placed where degenerate DNA bases coded for degenerate amino acids to avoid splicing difficulties later. Where this was too difficult some degenerate bases were removed according to the protein consensus design rules outlined above and indicated in Figure 12. Figure 16 shows an example of the oligonucleotides design for each subcassette.

Construction of the HIV Savine

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Five of each group of ten designed oligonucleotides were spliced together using stepwise asymmetric PCR (Sandhu et al., 1992) and Splicing by Overlap Extension (SOEing) (Figure 17a). Each subcassette was then PCR amplified, cloned into pBluescript™ II KS- using BamHI/EcoRI and 16 individual clones sequenced. Mutations, deletions and insertions were present in the large majority of the clones for each subcassette, despite acrylamide gel purification of the long oligonucleotides. In order to construct a functional Savine with minimal mutations, two clones for each subcassette with no insertions or deletions and hence a complete open reading frame and with minimal numbers of non-designed mutations, were selected from the sixteen available. The subcassettes were then excised from their plasmids and joined by stepwise PCR-amplified ligation using the polymerase blend ElongaseTM (Life Technology), T4 DNA ligase and the cohesive restriction enzymes XbaI/SpeI/AvrII/NheI, to generate two copies of cassettes A, B and C as outlined in Figure 14 and shown in Figure 17b. Predicted sequences for these cassettes are shown in Figure 30. Each cassette was then reamplified by PCR with Elongase[™], cloned into pBluescript[™] II KS⁻ and 3 of the resulting plasmid clones sequenced using 12 of the 36 sequencing primers designed to cover the full length construct. Clones with minimal or no further mutations were selected for transfer into plasmids for DNA vaccination or used to make recombinant poxviruses. A summary of the number of designed and non-designed mutations in each Savine construct is presented in Table 1.

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TABLE 1
Summary of mutations

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Construct	NT.	Number of mutations			
Construct	No. aas	Designed	Expected in 2 clones	Actual in 2	Non-designed
Cassette A	1896	249	124	107	5 (AC1), 8 (AC2)
Cassette B	1184	260	130	124	11 (BC1), 4 (BC2)
Cassette C	1969	276	138	121	10 (CC1), 14 (CC2)
Full length	5742	785	392	352	26 (FL1), 26 (FL2)

Summary of the mutations present in the two full-length clones constructed as determined by sequencing. Includes the number of mutations designed, expected and actually present in the 2 clones and the number of non-designed mutations in each cassette and full-length clone.

HIV Savine DNA vaccines and Recombinant Vaccinia viruses

To test the immunological effectiveness of the HIV Savine constructs the cassette sequences were transferred into DNA vaccine and poxvirus vectors. These vectors when used either separately in immunological assays described below or together in a 'prime-boost' protocol which has been shown previously to generate strong T cell responses in vivo (Kent et al., 1997).

DNA Vaccination plasmids were constructed by excising the cassettes from the selected plasmid clones with XbaI/XhoI (cassette A) or XbaI/SaII (cassettes B and C) and ligating them into pDNAVacc cut with XbaI/XhoI to create pDVAC1, pDVAC2, pDVBC1, pDVBC2, pDVCC1, pDVCC2, respectively (Figure 18a). These plasmids were then further modified by cloning into their XbaI site a DNA fragment excised using XbaI/AvrII from pTUMERA2 and encoding a synthetic endoplasmic reticulum (ER) signal sequence from the Adenovirus E1A protein (Persson et al., 1980) (Figure 18a). ER signal sequences have been shown previously to enhance the presentation of both CTL and T helper epitopes in vivo (Ishioka, G.Y., 1999; Thomson et al., 1998). The plasmids pDVERAC1, pDVERBC1, pDVERCC1 andpDVERAC2, pDVERBC2, pDVERCC2 were then mixed

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together to create, plasmid pool 1 and pool 2 respectively. Each plasmid pool collectively encodes one copy of the designed full-length HIV Savine.

Plasmids to generate recombinant Vaccinia viruses which express HIV Savine sequences were constructed by excising the various HIV Savine cassettes from the selected plasmid clones using *BamHI/XhoI* (cassette A) or *BamHI/SaII* (cassettes B and C) and cloned into the marker rescue plasmid, pTK7.5, cleaved with *BamHI/SaII*. These pTK7.5-derived plasmids were then used to generate recombinant Vaccinia viruses by marker rescue recombination using established protocols (Boyle *et al.*, 1985) to generate VV-AC1, VV-AC2, VV-BC1, VV-BC2, VV-CC1 and VV-CC2 (Figure 18b).

Two further DNA vaccine plasmids were constructed each encoding a version of the full length HIV Savine (Figure 18c). Briefly, the two versions of cassette B were excised with *Xho*I and cloned into the corresponding selected plasmid clones containing cassette A sequences that were cut with *Xho*I/SaII to generate pBSAB1 and pBSAB2 respectively. The joined A/B cassettes in pBSAB1 and pBSAB2 were excised with *Xba*I/XhoI and cloned into pDVCC1 and pDVCC2, respectively, and cleaved with *Xba*I/XhoI to generate pDVFL1 and pDVFL2. These were then further modified to contain an ER signal sequence using the same cloning strategy as outlined in figure 18a.

Restimulation of HIV specific lymphocytes from HIV infected patients

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The present inventors examined the capacity of the HIV Savine to restimulate HIV-specific polyclonal CTL responses from HIV-infected patients. PBMCs from three 20 different patients were restimulated in vitro with two HIV Savine Vaccinia virus pools (Pool 1 included VV-AC1 and VV-BC1; Pool 2 included VV-AC2, VV-BC2 and VV-CC2) then used in CTL lysis assays against LCLs infected either with one of the Savine Vaccinia virus pools or Vaccinia viruses which express gag, env or pol. Figure 19 clearly shows, 25 that in all three assays, both HIV Savine viral pools restimulated HIV-specific CTL responses which could recognise targets expressing whole natural HTV antigens and not targets which were uninfected or infected with the control Vaccinia virus. Furthermore, in all three cases, both pools restimulated responses that recognised all three natural HIV antigens. This result suggests that the combined Savine constructs will provide broader immunological coverage than single antigen based vaccine approaches. The level of lysis 30 in each case of targets infected with Savine viral pools was significantly higher than the

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lysis recorded for any other infected target. This probably reflects the combined CTL responses to gag, pol, and env plus other HIV antigens not analysed here but whose sequences are also incorporated into the Savine constructs.

CTL recognition of each HIV antigen is largely controlled by each patient's HLA background hence the pattern of CTL lysis for whole HIV antigens is different in each patient. Interestingly, this CTL lysis pattern did not change when the second Savine Vaccinia virus pool was used for CTL restimulation. In these assays, therefore, the inventors were unable to demonstrate clear differences between pools 1 and 2, despite pool 1 lacking a Vaccinia virus expressing cassette CC1 and despite the many amino acid differences between the A and B cassettes in each pool (see table 1).

From the foregoing, the present inventors have developed a novel vaccine/therapeutic strategy. In one embodiment, pathogen or cancer protein sequences are systemically fragmented, reverse translated back into DNA, rearranged randomly then joined back together. The designed synthetic DNA sequence is then constructed using long oligonucleotides and can be transferred into a range of delivery vectors. The vaccine vectors used here were DNA vaccine plasmids and recombinant poxvirus vectors which have been previously shown to elicit strong T cell responses when used together in a 'prime-boost' protocol (Kent et al., 1997). An important advantage of scrambled antigen vaccines or 'Savines' is that the amount of starting sequence information for the design can be easily expanded to include the majority of the protein sequences from a pathogen or for cancer, thereby providing the maximum possible vaccine or therapy coverage for a given population.

An embodiment of the systematic fragmentation approach described herein was based on the size and processing requirements for T cell epitopes and was designed to cause maximal disruption to the structure and function of protein sequences. This fragmentation approach ensures that the maximum possible range of T cell epitopes will be present from any incorporated protein sequence without the protein being functional and able to compromise vaccine safety

Another important advantage of Savines is that consensus protein sequences can be used for their design. This feature is only applicable when the design needs to cater for pathogen or cancer antigens whose sequence varies considerably. HIV is a highly

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mutagenic virus, hence this feature was utilised extensively to design a vaccine which has the potential to cover not only field isolates of HIV but also the major HIV clades involved in the current HIV pandemic. To construct the HIV Savine, one set of long oligonucleotides was synthesised, which included degenerate bases in such a way that 8 constructs are theoretically required for the vaccine to contain all combinations in any stretch of 9 amino acids. The inventors believe that this approach can be improved for the following reasons: 1) While degenerate bases should be theoretically equally represented, in practice some degenerate bases were biased towards one base or the other, leading to a lower than expected frequency of the designed mutations in the two full length HIV Savines which were constructed (see Table 1). 2) Only sequence combinations actually present in the HIV clade consensus sequences are required to get full clade coverage, hence the number of full length constructs needed could be reduced. To reduce the number of constructs however, separate sets of long oligonucleotides would have to be synthesised, significantly increasing the cost, time and effort required to generate a vaccine capable of such considerable vaccine coverage.

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A significant problem during the construction of the HIV Savine synthetic DNA sequence was the incorporation of non-designed mutations. The most serious types of mutations were insertions, deletions or those giving rise to stop codons, all of which change the frame of the synthesised sequences and/or caused premature truncation of the Savine proteins. These types of mutation were removed during construction of the HIV Savines by sequencing multiple clones after subcassette and cassette construction and selecting functional clones. The major source of these non-designed mutations was in the long oligonucleotides used for Savine synthesis, despite their gel purification. This problem could be reduced by making the initial subcassettes smaller thereby reducing the possibility of corrupted oligonucleotides being incorporated into each subcassette clone. The second major cause of non-designed mutations was the large number of PCR cycles required for the PCR and ligation-mediated joining of the subcassettes. Including extra sequencing and clone selection steps during the subcassette joining process should help to reduce the frequency of non-designed mutations in future constructs. Finally, another method that could help reduce the frequency of such mutations at all stages is to use resolvase treatment. Resolvases are bacteriophage-encoded endonucleases which recognise disruptions to double stranded DNA and are primarily used by bacteriophages to resolve

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Holliday junctions (Mizuuchi, 1982; Youil et al., 1995). T7 endonuclease I has already been used by the present inventors in synthetic DNA constructions to recognise mutations and cleave corrupted dsDNA to allow gel purification of correct sequences. Cleavage of corrupted sequences occurs because after a simple denaturing and hybridisation step mutated DNA hybridises to correct DNA sequences and results in a mispairing of DNA bases which is able to be recognised by the resolvase. This method resulted in a 50% reduction in the frequency of errors. Further optimisation of this method and the use of a thermostable version of this type of enzyme could further reduce the frequency of errors during long Savine construction.

Two pools of Vaccinia viruses expressing Savine cassettes were both shown to restimulate HIV-specific responses from three different patients infected with B clade HIV viruses. These results provide a clear indication that the HIV Savine should provide broad coverage of the population because each patient had a different HLA pattern yet both pools were able to restimulate HIV-specific CTL responses in all three patients against all three natural HIV proteins tested. Also, both pools were shown to restimulate virtually identical CTL patterns in all three patients. This result was unexpected because some responses should have been lost or gained due to the amino acid differences between the two pools and because Pool 1 is only capable of expressing 2/3 of the full length HIV Savine. There are two suggested reasons why the pattern of CTL lysis was not altered between the two viral pools. Firstly, the sequences in the Savine constructs are nearly all duplicated because the fragment sequences overlap. Hence the loss of a third of the Savine may not have excluded sufficient T cell epitopes for differences to be detected in only three patient samples against only three HIV proteins. Secondly, while mutations often destroy T cell epitopes, if they remain functional, then the CTL they generate frequently can recognise alternate epitope sequences. Taken together this finding indirectly suggests that combining only two Savine constructs may provide robust multiclade coverage. Further experiments are being carried out to directly examine the capacity of the HIV Savine to stimulate CTL generated by different strains of HIV virus. The capacity of the two HIV-1 Savine Vaccinia vector pools to stimulate CD4+ T cell HIV-1 specific responses from infected patients was also tested (Figure 20). Both patients showed significant proliferation of CD4+ T cells although both pools did not show consistent patterns suggesting that the two pools may provide wider vaccine coverage than using either pool independently.

The present inventors have generated a novel vaccine strategy, which has been used to generate what the inventors believe to be the most effective HIV candidate vaccine to date. The inventors have used this vaccine to immunise naive mice. Figure 21 shows conclusively that the HIV-1 Savine described above can generate a Gag and Nef CTL response in naïve mice. It should be noted, however, that the Nef CTL epitope appeared to exist only in Pool 1 since it was not restimulated by Pool 2. This is further proof of the utility of combining HIV-1 Savine Pool 1 and Pool 2 components together to provide broader vaccine coverage.

The HIV-1 Savine Vaccinia vectors have also been used to restimulate *in vivo* HIV-1 responses in pre-immune *M. nemestrina* monkeys. These experiments (Figure 22) showed, by INF-γ ELISPOT and CD69 expression on both CD4 and CD8 T cells, that the ability of the HIV-1 SAVINE to restimulate HIV-1 specific responses in vivo is equivalent or perhaps better than another HIV-1 candidate vaccine.

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This is a generic strategy able to be applied to many other human infections or cancers where T-cell responses are considered to be important for protection or recovery. With this in mind the inventors have begun constructing Savines for melanoma, cervical cancer and Hepatitis C. In the case of melanoma, the majority of the currently identified melanoma antigens have been divided into two groups, one containing antigens associated with melanoma and one containing differentiation antigens from melanocytes, which are often upregulated in melanomas. Two Savine constructs are presently being constructed to cater for these two groups. The reason for making the distinction is that treatment of melanoma might first proceed using the Savine that incorporates fragments of melanoma specific antigens only. If this Savine fails to control some metastases then the less specific Savine containing the melanocyte-specific antigens can then be used. It is important to point out that other cancers also express many of the antigens specific to melanomas e.g., testicular and breast cancers. Hence the melanoma specific Savine may have therapeutic benefits for other cancers.

A small Savine is also being constructed for cervical cancer. This Savine will contain two antigens, E6 and E7, from two strains of human papilloma virus (HPV), HPV-16 and HPV-18, directly linked with causing the majority of cervical cancers worldwide. There is a large number of sequence differences in these two antigens between the two

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strains which would normally require two Savines to be constructed. However since this Savine is small, the antigen fragments from both strains are being scrambled together. While it is normally better for the Savine approach to include all or a majority of the antigens from a virus, in this case only E6 and E7 are expressed during viral latency or in cervical carcinomas. Hence in the interests of simplicity, the rest of the HPV genome will not be included although all HPV antigens would be desirable in a Savine against genital warts.

Two Savines have also been constructed for two strains of hepatitis C, a major cause of liver disease in the world. Hepatitis C is similar to HIV in the requirements for a vaccine or therapeutic. However, the major hepatitis C strains share significantly lower homology, 69-79%, with one another than do the various HIV clades. To cater for this the inventors have decided to construct two separate constructs to cater for the two major strains present in Australia, types 1aand 3a, which together cause approximately 80-95% of hepatitis C infections in this country. Both constructs will be approximately the same size as the HIV Savine but will be blended together into a single vaccine or therapy.

Overall it is believed that the Savine vaccine strategy is a generic technology likely to be applied to a wide range of human diseases. It is also believed that because it is not necessary to characterise each antigen, this technology will be actively applied to animal vaccines as well where research into vaccines or therapies is often inhibited by the lack of specific reagents, modest research budgets and poor returns on animal vaccines.

EXAMPLE 2

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Hepatitis C Savine

Synthetic immunomodulatory molecules have also been designed for treating Hepatitis C. In one example, the algorithm of Figure 25 was applied to a consensus polyprotein sequence of Hepatitis C 1a to facilitate its segmentation into overlapping segments (30 aa segments overlapping by 15 aa), the rearrangement of these segments into a scrambled order and the output of Savine nucleic acid and amino acid sequences, as shown in Figure 26. Exemplary DNA cassettes (A, B and C) are also shown in Figure 26, which contain suitable restriction enzyme sites at their ends to facilitate their joining into a single expressible open reading frame.

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EXAMPLE 3

Melanoma Savine

The algorithm of Figure 25 was also applied to melanocyte differentiation antigens (gp100, MART, TRP-1, Tyros, Trp-2, MC1R, MUC1F and MUC1R) and to melanoma specific antigens (BAGE, GAGE-1, gp100In4, MAGE-1, MAGE-3, PRAME, TRP2IN2, NYNSO1a, NYNSO1b and LAGE1), as shown in Figure 27, to provide separate Savine nucleic acid and amino acid sequences for treating or preventing melanoma.

EXAMPLE 4

Resolvase Repair Experiment

A resolvase can be used advantageously to repair errors in polynucleotides. The following procedure outlines resolvase repair of a synthetic 340 bp fragment in which DNA errors were common.

Method

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The 340 bp fragment was PCR amplified and gel purified on a 4% agarose gel. After spin purifying, 10ul of the eluate corresponding to approximately 100 ng was subjected to the resolvase repair treatment. The rest of the DNA sample was stored for later cloning as the untreated control.

 $2~\mu L$ of 10xPCR buffer, $2~\mu L$ of 20 mM MgCl₂ and $6~\mu L$ of MilliQTM water (MQW) and Taq DNA polymerase were added to the $10~\mu L$ DNA sample. The mixture was subjected to the following thermal profile; $95^{\circ}C$ for 5min, $65^{\circ}C$ for 30min, cooled and held at $37^{\circ}C$. Five μL of 10xT7 endonuclease I buffer, $8~\mu L$ of $1/50~\mu L$ of T7endoI enzyme stock and $17~\mu L$ of MQW were added, mixed and incubated for $30~\min$. Loading buffer was added to the sample and the sample was electrophoresed on a 4% agarose gel. A faint band corresponding to the full length fragment was excised and subjected to 15~further cycles of PCR. The amplified fragment was agarose gel purified and, along with the untreated DNA sample, cloned into pBluescript. Eleven plasmid clones for each DNA sample were sequenced and the number and type of errors compared (see table)

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Buffers were as follows:

10x T7endonuclease buffer

2.5ml 1M TRIS pH7.8, 0.5ml 1M MgCl₂, 25 μ L 1 M DTT, 50 μ L 10mg/mL BSA, 2 mL MQW made up to a total of 5 mL.

5 T7 endonuclease I stock

Concentrated sample of enzyme prepared by, and obtained from, Jeff Babon (St Vincent's Hospital) was diluted 1/50 using the following dilution buffer: 50 μ L 1 M TRIS pH7.8, 0.1 μ L 1M EDTA pH8, 5 μ L 100 mM glutathione, 50 μ L 10mg/mL BSA, 2.3 mL MQW, 2.5 mL glycerol made up to a total of 5 mL.

10 Results

The results are summarised in Tables 2 and 3.

TABLE 2

Total Errors				
Untreated	Resolvase treated			
A/T to $G/C = 6$	A/T to $G/C = 1$			
G/C to $A/T = 12$	G/C to $A/T = 7$			
A/T to deletion = 1	A/T to deletion = 1			
G/C to deletion = 6	G/C to deletion = 3			

TABLE 3

Clone summary				
Untreated	Resolvase treated			
6/11 contained deletions	3/11 contained deletions			
9/11 contained mutations	7/11 contained mutations			

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Clone si	ummary
Untreated	Resolvase treated
2/11 correct	3/11 correct

<u>Discussion/Conclusion</u>

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While overall the number of correct clones obtained was not significantly different, there was a significant difference in the level of errors. This reduction in errors becomes more significant as greater numbers of long oligonucleotides are joined into the one construct *i.e.*, increasing the difference between untreated *versus* treated samples in the chance of obtaining a correct clone. It is believed that combining another resolvase such as T4 endonuclease VII may further enhance repair or increase the bias against errors.

Importantly, this experiment was not optimised e.g., by using proofreading PCR enzymes or optimised conditions. Finally if the repair reaction is carried out during normal PCR, for example, by including a thermostable resolvase, it is believed that amplification of already damaged long oligonucleotides, and the normal accumulation of PCR induced errors, even using error reading polymerases during PCR, could be reduced significantly. The repair of damaged long oligonucleotides is particularly important for synthesis of long DNA fragment such as in Savines because, while the rate of long oligonucleotide damage is typically <5%, after joining 10 oligonucleotides, the error rate approaches 50%. This is true even using the best proofreading PCR enzymes because these enzymes do not verify the sequence integrity using correct oligonucleotide templates that exist as a significant majority (95%) in a joining reaction.

The disclosure of every patent, patent application, and publication cited herein is incorporated herein by reference in its entirety.

The citation of any reference herein should not be construed as an admission that such reference is available as "Prior Art" to the instant application

Throughout the specification the aim has been to describe the preferred embodiments of the invention without limiting the invention to any one embodiment or specific collection of features. Those of skill in the art will therefore appreciate that, in

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light of the instant disclosure, various modifications and changes can be made in the particular embodiments exemplified without departing from the scope of the present invention. All such modifications and changes are intended to be included within the scope of the appended claims.

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WHAT IS CLAIMED IS:

- 1. A synthetic polypeptide comprising a plurality of different segments of at least one parent polypeptide, wherein the segments are linked together in a different relationship relative to their linkage in the at least one parent polypeptide to impede, abrogate or otherwise alter at least one function associated with the parent polypeptide.
- 2. The synthetic polypeptide of claim 1, consisting essentially of different segments of a single parent polypeptide.
- 3. The synthetic polypeptide of claim 1, consisting essentially of different segments of a plurality of different parent polypeptides.
- 4. The synthetic polypeptide of claim 1, wherein the segments in said synthetic polypeptide are linked sequentially in a different order or arrangement relative to their linkage in said at least one parent polypeptide.
- 5. The synthetic polypeptide of claim 4, wherein the segments in said synthetic polypeptide are randomly rearranged relative to their order or arrangement in said at least one parent polypeptide.
- 6. The synthetic polypeptide of claim 1, wherein the size of an individual segment is at least 4 amino acids.
- 7. The synthetic polypeptide of claim 6, wherein the size of an individual segment is from about 20 to about 60 amino acids.
- 8. The synthetic polypeptide of claim 7, wherein the size of an individual segment is about 30 amino acids.
- 9. The synthetic polypeptide of claim 7, comprising at least 30% of the parent polypeptide sequence.
- 10. The synthetic polypeptide of claim 1, wherein at least one of said segments comprises partial sequence identity or homology to one or more other said segments.
- 11. The synthetic polypeptide of claim 10, wherein the sequence identity or homology is contained at one or both ends of an individual segment.

- 12. The synthetic polypeptide of claim 11, wherein one or both ends of said segment comprises at least 4 contiguous amino acids that are identical to, or homologous with, an amino acid sequence contained within one or more other of said segments.
- 13. The synthetic polypeptide of claim 10, wherein the size of an individual segment is about twice the size of the sequence that is identical or homologous to the or each other said segment.
- 14. The synthetic polypeptide of claim 13, wherein the size of an individual segment is about 30 amino acids and the size of the sequence that is identical or homologous to the or each other said segment is about 15 amino acids.
- 15. The synthetic polypeptide of claim 1, wherein an optional spacer is interposed between some or all of the segments.
- 16. The synthetic polypeptide of claim 15, wherein the spacer alters proteolytic processing and/or presentation of adjacent segment(s).
- 17. The synthetic polypeptide of claim 16, wherein the spacer comprises at least one neutral amino acid.
- 18. The synthetic polypeptide of claim 16, wherein the spacer comprises at least one alanine residue.
- 19. The synthetic polypeptide of claim 1, wherein the at least one parent polypeptide is associated with a disease or condition.
- 20. The synthetic polypeptide of claim 1, wherein the at least one parent polypeptide is selected from a polypeptide of a pathogenic organism, a cancer-associated polypeptide, an autoimmune disease-associated polypeptide, an allergy-associated polypeptide or a variant or derivative of these.
- 21. The synthetic polypeptide of claim 1, wherein the at least one parent polypeptide is a polypeptide of a virus.
- 22. The synthetic polypeptide of claim 21, wherein the virus is selected from a Human Immunodeficiency Virus (HIV) or a Hepatitis virus.
- 23. The synthetic polypeptide of claim 22, wherein the virus is a Human Immunodeficiency Virus (HIV) and the at least one parent polypeptide is selected from env, gag, pol, vif, vpr, tat, rev, vpu and nef, or a combination thereof.

- 24. The synthetic polypeptide of claim 1, wherein the at least one parent polypeptide is a cancer-associated polypeptide.
- 25. The synthetic polypeptide of claim 24, wherein the cancer is melanoma.
- 26. The synthetic polypeptide of claim 25, wherein the at least one parent polypeptide is a melanocyte differentiation antigen.
- 27. The synthetic polypeptide of claim 25, wherein the at least one parent polypeptide is a melanocyte differentiation antigen selected from gp100, MART, TRP-1, Tyros, TRP2, MC1R, MUC1F, MUC1R or a combination thereof.
- 28. The synthetic polypeptide of claim 25, wherein the at least one parent polypeptide is a melanoma-specific antigen.
- 29. The synthetic polypeptide of claim 25, wherein the at least one parent polypeptide is a melanoma-specific antigen selected from BAGE, GAGE-1, gp100In4, MAGE-1, MAGE-3, PRAME, TRP2IN2, NYNSO1a, NYNSO1b, LAGE1 or a combination thereof.
- 30. A synthetic polynucleotide encoding a synthetic polypeptide comprising a plurality of different segments of at least one parent polypeptide, wherein the segments are linked together in a different relationship relative to their linkage in the at least one parent polypeptide to impede, abrogate or otherwise alter at least one function associated with the parent polypeptide.
- 31. A method for producing the synthetic polynucleotide encoding a synthetic polypeptide comprising a plurality of different segments of at least one parent polypeptide, wherein the segments are linked together in a different relationship relative to their linkage in the at least one parent polypeptide to impede, abrogate or otherwise alter at least one function associated with the parent polypeptide, said method comprising:
 - linking together in the same reading frame a plurality of nucleic acid sequences encoding different segments of the at least one parent polypeptide to form a synthetic polynucleotide whose sequence encodes said segments linked together in a different relationship relative to their linkage in the at least one parent polypeptide.
- 32. The method of claim 31, further comprising fragmenting the sequence of a respective parent polypeptide into fragments and linking said fragments together in a different relationship relative to their linkage in a respective parent polypeptide sequence.

- 33. The method of claim 32, wherein the fragments are randomly linked together.
- 34. The method of claim 31, further comprising reverse translating the sequence of a respective parent polypeptide or a segment thereof to provide a nucleic acid sequence encoding said parent polypeptide or said segment.
- 35. The method of claim 34, wherein an amino acid of a respective parent polypeptide sequence is reverse translated to provide a codon, which has higher translational efficiency than other synonymous codons in a cell of interest.
- 36. The method of claim 35, wherein an amino acid of said parent polypeptide sequence is reverse translated to provide a codon which, in the context of adjacent or local sequence elements, has a lower propensity of forming an undesirable sequence that is refractory to the execution of a task.
- 37. The method of claim 35, wherein an amino acid of said parent polypeptide sequence is reverse translated to provide a codon which, in the context of adjacent or local sequence elements, has a lower propensity of forming an undesirable sequence selected from a palindromic sequence or a duplicated sequence, which is refractory to the execution of a task selected from cloning or sequencing.
- 38. The method of claim 31, further comprising linking a spacer oligonucleotide encoding at least one spacer residue between segment-encoding nucleic acids.
- 39. The method of claim 38, wherein spacer oligonucleotide encodes 2 to 3 spacer residues.
- 40. The method of claim 38 or claim 39, wherein the spacer residue is a neutral amino acid.
- 41. The method of claim 38 or claim 39, wherein the spacer residue is alanine.
- 42. The method of claim 31, further comprising linking in the same reading frame as other segment-containing nucleic acid sequences at least one variant nucleic acid sequence which encodes a variant segment having a homologous but not identical amino acid sequence relative to other encoded segments.

- 43. The method of claim 42, wherein the variant segment comprises conserved and/or non-conserved amino acid differences relative to one or more other encoded segments.
- 44. The method of claim 43, wherein the differences correspond to sequence polymorphisms.
- 45. The method of claim 44, wherein degenerate bases are designed or built in to the at least one variant nucleic acid sequence to give rise to all desired homologous sequences.
- 46. The method of claim 31, further comprising optimising the codon composition of the synthetic polynucleotide such that it is translated efficiently by a host cell.
- 47. A synthetic construct comprising a synthetic polynucleotide encoding a synthetic polypeptide comprising a plurality of different segments of at least one parent polypeptide, wherein the segments are linked together in a different relationship relative to their linkage in the at least one parent polypeptide to impede, abrogate or otherwise alter at least one function associated with the parent polypeptide, wherein said synthetic polynucleotide is operably linked to a regulatory polynucleotide.
- 48. The synthetic construct of claim 47, further including a nucleic acid sequence encoding an immunostimulatory molecule.
- 49. The synthetic construct of claim 48, wherein the immunostimulatory molecule comprises a domain of an invasin protein (Inv).
- 50. The synthetic construct of claim 48, wherein the immunostimulatory molecule comprises the sequence set forth in SEQ ID NO: 1467 or an immune stimulatory homologue thereof.
- 51. The synthetic construct of claim 48, wherein the immunostimulatory molecule is a T cell co-stimulatory molecule.
- 52. The synthetic construct of claim 48, wherein the immunostimulatory molecule is a T cell co-stimulatory molecule selected from a B7 molecule or an ICAM molecule.
- 53. The synthetic construct of claim 48, wherein the immunostimulatory molecule is a B7 molecule or a biologically active fragment thereof, or a variant or derivative of these.

- 54. The synthetic construct of claim 48, wherein the immunostimulatory molecule is a cytokine selected from an interleukin, a lymphokine, tumour necrosis factor or an interferon.
- 55. The synthetic construct of claim 48, wherein the immunostimulatory molecule is an immunomodulatory oligonucleotide.
- 56. An immunopotentiating composition, comprising an immunopotentiating agent selected from the synthetic polypeptide of claim 1, the synthetic polynucleotide of claim 30 or the synthetic construct of claim 47, together with a pharmaceutically acceptable carrier.
- 57. The composition of claim 56, further comprising an adjuvant.
- 58. A method for modulating an immune response, which response is preferably directed against a pathogen or a cancer, comprising administering to a patient in need of such treatment an effective amount of an immunopotentiating agent selected from the synthetic polypeptide of claim 1, the synthetic polynucleotide of claim 30, the synthetic construct of claim 47, or the composition of claim 56.
- 59. A method for treatment and/or prophylaxis of a disease or condition, comprising administering to a patient in need of such treatment an effective amount of an immunopotentiating agent selected from selected from the synthetic polypeptide of claim 1, the synthetic polynucleotide of claim 30, the synthetic construct of claim 47, or the composition of claim 56.
- 60. A computer program product for designing the sequence of a synthetic polypeptide comprising a plurality of different segments of at least one parent polypeptide, wherein the segments are linked together in a different relationship relative to their linkage in the at least one parent polypeptide to impede, abrogate or otherwise alter at least one function associated with the parent polypeptide, said program product comprising:
 - code that receives as input the sequence of said at least one parent polypeptide;
 - code that fragments the sequence of a respective parent polypeptide into fragments;
 - code that links together said fragments in a different relationship relative to their linkage in said parent polypeptide sequence; and

- a computer readable medium that stores the codes.
- 61. The computer program product of claim 60, further comprising code that randomly rearranges said fragments.
- 62. The computer program product of claim 60, further comprising code that links the sequence of a spacer residue to the sequence of said at least one parent polypeptide or to said fragments.
- 63. A computer program product for designing the sequence of a synthetic polynucleotide encoding a synthetic polypeptide comprising a plurality of different segments of at least one parent polypeptide, wherein the segments are linked together in a different relationship relative to their linkage in the at least one parent polypeptide to impede, abrogate or otherwise alter at least one function associated with the parent polypeptide, comprising:
 - code that receives as input the sequence of at least one parent polypeptide;
 - code that fragments the sequence of a respective parent polypeptide into fragments;
 - code that reverse translates the sequence of a respective fragment to provide a nucleic acid sequence encoding said fragment;
 - code that links together in the same reading frame each said nucleic acid sequence to provide a polynucleotide sequence that codes for a polypeptide sequence in which said fragments are linked together in a different relationship relative to their linkage in the at least one parent polypeptide sequence; and
 - a computer readable medium that stores the codes.
- 64. The computer program product of claim 63, further comprising code that randomly rearranges said nucleic acid sequences.
- 65. The computer program product of claim 64, further comprising code that reverse translates an amino acid of a respective parent polypeptide sequence to provide a codon, which has higher translational efficiency than other synonymous codons in a cell of interest.
- 66. The computer program product of claim 63, further comprising code that reverse translates an amino acid of a respective parent polypeptide sequence to provide a codon

which, in the context of adjacent or local sequence elements, has a lower propensity of forming an undesirable sequence that is refractory to the execution of a task.

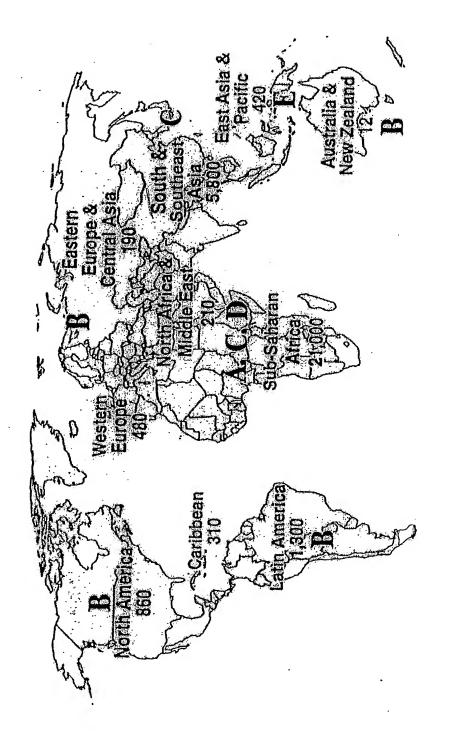
- 67. The computer program product of claim 63, further comprising code that links a spacer oligonucleotide to one or more of said nucleic acid sequences.
- 68. A computer for designing the sequence of a synthetic polypeptide comprising a plurality of different segments of at least one parent polypeptide, wherein the segments are linked together in a different relationship relative to their linkage in the at least one parent polypeptide to impede, abrogate or otherwise alter at least one function associated with the parent polypeptide, wherein said computer comprises:
 - (a) a machine-readable data storage medium comprising a data storage material encoded with machine-readable data, wherein said machine-readable data comprise the sequence of at least one parent polypeptide;
 - (b) a working memory for storing instructions for processing said machine-readable data;
 - (c) a central-processing unit coupled to said working memory and to said machinereadable data storage medium, for processing said machine readable data to provide said synthetic polypeptide sequence; and
 - (d) an output hardware coupled to said central processing unit, for receiving said synthetic polypeptide sequence.
- 69. The computer of claim 68, wherein the processing of said machine readable data comprises fragmenting the sequence of a respective parent polypeptide into fragments and linking together said fragments in a different relationship relative to their linkage in the sequence of said parent polypeptide.
- 70. The computer of claim 68, wherein the processing of said machine readable data comprises randomly rearranging said fragments.
- 71. The computer of claim 68, wherein the processing of said machine readable data comprises linking the sequence of a spacer residue to the sequence of said at least one parent polypeptide or to said fragments.

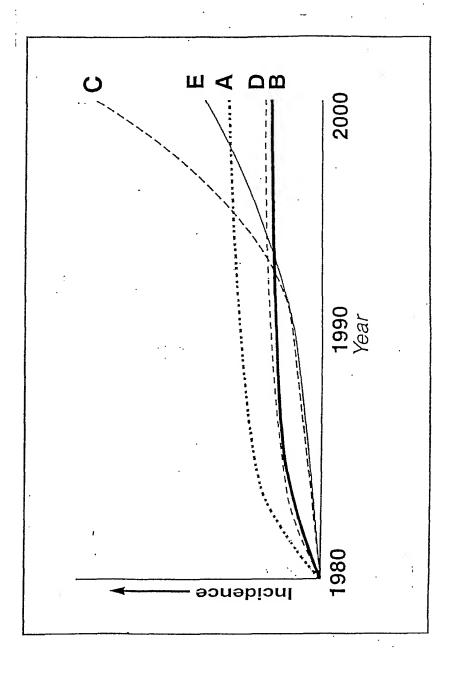
- 72. A computer for designing the sequence of a synthetic polynucleotide encoding a synthetic polypeptide comprising a plurality of different segments of at least one parent polypeptide, wherein the segments are linked together in a different relationship relative to their linkage in the at least one parent polypeptide to impede, abrogate or otherwise alter at least one function associated with the parent polypeptide, wherein said computer comprises:
 - (a) a machine-readable data storage medium comprising a data storage material encoded with machine-readable data, wherein said machine-readable data comprise the sequence of at least one parent polypeptide;
 - (b) a working memory for storing instructions for processing said machine-readable data;
 - (c) a central-processing unit coupled to said working memory and to said machinereadable data storage medium, for processing said machine readable data to provide said synthetic polynucleotide sequence; and
 - (d) an output hardware coupled to said central processing unit, for receiving said synthetic polynucleotide sequence.
- 73. The computer of claim 72, wherein the processing of said machine readable data comprises fragmenting the sequence of a respective parent polypeptide into fragments, reverse translating the sequence of a respective fragment to provide a nucleic acid sequence encoding said fragment and linking together in the same reading frame each said nucleic acid sequence to provide a polynucleotide sequence that codes for a polypeptide sequence in which said fragments are linked together in a different relationship relative to their linkage in the at least one parent polypeptide sequence.
- 74. The computer of claim 72, wherein the processing of said machine readable data comprises randomly rearranging said nucleic acid sequences.
- 75. The computer of claim 72, wherein the processing of said machine readable data comprises reverse translating an amino acid of a respective parent polypeptide sequence to provide a codon, which has higher translational efficiency than other synonymous codons in a cell of interest.

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76. The computer of claim 72, wherein the processing of said machine readable data comprises reverse translating an amino acid of a respective parent polypeptide sequence to provide a codon which, in the context of adjacent or local sequence elements, has a lower propensity of forming an undesirable sequence that is refractory to the execution of a task.

77. The computer of claim 72, wherein the processing of said machine readable data comprises linking a spacer oligonucleotide to one or more of said nucleic acid sequences.





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1	o17 -> /<- nls ->/ /<- membrane binding ->/	
DESIGNED SE	O MGARASVLSGGKLDAWEKIRLRPGGKKKYKMKHLVWASRELERFALNPGLLETAEGCQQILEQLQSALKT R E RL I S S K G P Q	70
E-ISOLATE	MGARASVLSGGKLDAWEKIRLRPGGKKKYKMKHLVWASRELERFALNPGLLETAEGCQQLIEQLQSTLKT	70
CONSENSUS-A CONSENSUS-B CONSENSUS-D CONSENSUS-F CONSENSUS-G CONSENSUS-H CONSENSUS-O CONSENSUS-C		70 70 69 68 70 63 64 62 42
	/<- nls ->/	
DESIGNED SEC MUTATED AAS	Q GSEELKSLYNTIATLWCVHQRIEVKDTKEALDKIEEEQKKSQQKTQQAAADT.GSSSKV T R F V D R V N K N . Q	
E-ISOLATE	GSEELKSLYNTIATLWCVHQRIEVKDTKEALDKIEEVQKKSQQKKQQAAADT.GSSSKV	
CONSENSUS-A CONSENSUS-B CONSENSUS-D CONSENSUS-F CONSENSUS-F CONSENSUS-H CONSENSUS-O CONSENSUS-O	<pre>g?eElkSLfNtvatLycvHqrIdvkDtKeAldkiEeiqnKskqk??????tqqaaA?T.gs?sskv -sr-y</pre>	126 128 120 125 123 110 106 106
•	p17 \/ p24	
	b1, // b54	•
DESIGNED SEQ	The state of the s	•
	SQNYPIVQNAQGQMVHQPLSPRTLNAWVKVIEEKGFNPEVIPMFSALSEGATPQDLNMMLNIVGGH	
MUTATED AAs	SQNYPIVQNAQGQMVHQPLSPRTLNAWVKVIEEKGFNPEVIPMFSALSEGATPQDLNMMLNIVGGH L AI V AS T T T SQNYPIVQNAQGQMVHQPLSPRTLNAWVKVIEEKGFNPEVIPMFSALSEGATPQDLNMMLNIVGGH ????SqNYPIVQNaqgQm?hQ?lSPrTLnAwVKviEekaFspEVIPmFsaLSEGATPQdLNmMLNiVgGHTT	190 194 185 191 188 174 170 168 107
MUTATED AAS E-ISOLATE CONSENSUS-A CONSENSUS-B CONSENSUS-C CONSENSUS-F CONSENSUS-G CONSENSUS-H CONSENSUS-O CONSENSUS-O	SQNYPIVQNAQGQMVHQPLSPRTLNAWVKVIEEKGFNPEVIPMFSALSEGATPQDLNMMLNIVGGH L AI V AS T T T SQNYPIVQNAQGQMVHQPLSPRTLNAWVKVIEEKGFNPEVIPMFSALSEGATPQDLNMMLNIVGGH ????SqNYPIVQNaqgQm?hQ?lSPrTLnAwVKviEekaFspEVIPmFsaLSEGATPQdLNmMLNiVgGHTT	194 185 191 188 174 170
MUTATED AAS E-ISOLATE CONSENSUS-A CONSENSUS-B CONSENSUS-C CONSENSUS-F CONSENSUS-G CONSENSUS-H CONSENSUS-O CONSENSUS-O CONSENSUS-CP:	SQNYPIVQNAQGQMVHQPLSPRTLNAWVKVIEEKGFNPEVIPMFSALSEGATPQDLNMMLNIVGGH L AI V AS T T T SQNYPIVQNAQGQMVHQPLSPRTLNAWVKVIEEKGFNPEVIPMFSALSEGATPQDLNMMLNIVGGH ????SqNYPIVQNaqgQm?hQ?lSPrTLnAwVKviEekaFspEVIPmFsaLSEGATPQdLNmMLNIVGGH lv.ai	194 185 191 188 174 170
MUTATED AAS E-ISOLATE CONSENSUS-A CONSENSUS-B CONSENSUS-F CONSENSUS-F CONSENSUS-H CONSENSUS-H CONSENSUS-O CONSENSUS-O CONSENSUS-O CONSENSUS-O DESIGNED SEQ MUTATED AAS E-ISOLATE CONSENSUS-A CONSENSUS-B CONSENSUS-C CONSENSUS-F CONSENSUS-F CONSENSUS-G CONSENSUS-G CONSENSUS-H	SQNYPIVQNAQGQMVHQPLSPRTLNAWVKVIEEKGFNPEVIPMFSALSEGATPQDLNMMLNIVGGH L AI V AS T T T SQNYPIVQNAQGQMVHQPLSPRTLNAWVKVIEEKGFNPEVIPMFSALSEGATPQDLNMMLNIVGGH ????SqNYPIVQNaqgQm?hQ?lSPTLNAWVKViEekaFspEVIPMFsaLSEGATPQdLNmMLNIVGGH	194 185 191 188 174 170

FIGURE 3
SUBSTITUTE SHEET (RULE 26)

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						Zn-mo	
		p24	\/ \/	'p2'	\/ p7	/<-	-
DESIGNED SEQ MUTATED AAs	SILKALGTGATLEEMMTAC T R P S	G	v				
ISOLATE-E	SILKALGTGATLEEMMTAC						
CONSENSUS-A CONSENSUS-B CONSENSUS-C CONSENSUS-D CONSENSUS-F CONSENSUS-G CONSENSUS-H CONSENSUS-O CONSENSUS-CP2	sILraLg?gAtLeEMMTa T-KPa		a. a. A. ?2,20	. nn . tn . s - ta . Tn ?a sg A - 1 . Tn ?A DDLKGGYT/	s- aks- K?? ?K	K-piv K-prki K-R-iv K-P??? K-R-I? N.P?R-G	382 390 386 360 353 358
	ZII-MOCIL >/	/<-Zn-motif -		// 'I	-	\/ p6	
DESIGNED SEQ MUTATED AAS	CGKEGHLARNCRAPRKKGC I K	R		S			
ISOLATE-E	CGKEGHLARNCRAPRKKGC						
CONSENSUS - A CONSENSUS - C CONSENSUS - D CONSENSUS - F CONSENSUS - G CONSENSUS - H CONSENSUS - O CONSENSUS - O	}					-L	443 453 439 449 445 414 406 411 306
33	vpr binding				1	pr binding	p6
	/<>/	`\/ (minor)	(mir	nor) \/	/<>/	erminus / (80%)
DESIGNED SEQ MUTATED AAs	EPTAPPAE	NF.GFGEETT S R	.pspk(Q	P	KEHYPPSA L L	SLKSLFGNDPLSQ S	
ISOLATE-E	EPTAPPAE	NW.GMGEE		.QKD	KEHPPPSV	SLKSLFGNDPLSQ	•
CONSENSUS-A CONSENSUS-B CONSENSUS-C CONSENSUS-D CONSENSUS-F CONSENSUS-G CONSENSUS-H CONSENSUS-O CONSENSUS-CPZ	EPtAPpAE ?????e- ????????????	srft- ????SrFt- sF ????	-tps????q- pa Psq- Ps ?s P	pi p??- ??- P?? ?G	1Y?a	arx a	-\$ 500 479 - 495 482 440 436 444

CONSENSUS A-CPZ FROM LOS ALAMOS HIV SEQUENCE DATABASE ISOLATE-E SEQ FROM ISOLATE 93TH253 THAILAND

Underlined AA are not present in all overlapping segments

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DESIGNED SEQ MUTATED AAS	FFRE.NLAFQQGKAREFSSEQTGANSSASRKLGDGGGAERQ P E P R PT D	
ISOLATE-E	FFRE.NLAFQQGKAREFSSEQTGANSSASRKLGDGGGAERQ	
CONSENSUS-A CONSENSUS-B ISOLATE-C CONSENSUS-D CONSENSUS-O CONSENSUS-U CONSENSUS-CP2	FFRE.NLAFQQGEAR?F	35 49 48 35 48 13
	protease	
DESIGNED SEQ MUTATED AAS	<pre>- \/ <- gag cds end GTSSSFSFPQITLWQRPLVTIKIGGQLKEALLDTGADDTVLEDINLPGKWKPKMIGGIGGFIKVRQYD</pre>	
ISOLATE-E	GTSSSFSFPQITLWQRPLVTIKIGGQLKEALLDTGADDTVLEDINLPGKWKPKMIGGIGGFIKVRQYD	
CONSENSUS-A CONSENSUS-B	G???SF?FPQITLWQRPLVTV?I?GQLIEALLDTGADDTVLEDINLPGKWKPK?IGGIGGFIKVRQYDtVsik-gK	96 116
ISOLATE-C CONSENSUS-D CONSENSUS-O CONSENSUS-U	TV-n	115 94 115 55
CONDENSES, SE	protease \/ p66, p51	
DESIGNED SEQ MUTATED AAS	QILIEICGKKAIGTVLVGPTPVNIIGRNMLTQIGCTLNFPISPIDTVPVKLKPGMDGPKVKQWPLTEEKI I H E E	
ISOLATE-E	QILIEICGKKAIGTVLVGPTPVNIIGRNMLTQIGCTLNFPISPIDTVPVKLKPGMDGPKVKQWPLTEEKI	
CONSENSUS-A CONSENSUS-B	QILIEICGKK?IGTVLVGPTPVNIIGRNMLTQIGCTLNFPISPIETVPVKLKP?MDGPKVKQWPLTEEKI	164 186
ISOLATE-C		184
CONSENSUS-D	I	159
CONSENSUS-O		185
CONSENSUS-U CONSENSUS-CPZ	??	106
	M41L D67N K70R	
	KALTEICKEMEEEGKISKIGPENPYNTPVFAIKKKDSTKWRKLVDFRELNKRTQDFWEVQLGIPHPAGLK	
MUTATED AAS	A T K R I	
ISOLATE-E	KALTEICKEMEEEGKISKIGPENPYNTPVFAIKKKDSTKWRKLVDFRELNKRTQDFWEVQLGIPHPAGLK	
CONSENSUS-A CONSENSUS-B	KALT?IC?EMEKEGKISKIGPENPYNTPVFAIKKKDSTKWRKLVDFRELNKRTQDFWEVQLGIPH?AGLK	231 256
ISOLATE-C	vET	254
CONSENSUS-D	E-T	227
	TO N CO	

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DESIGNED SEQ QPIELPEKDSWTVNDIQKLVGKLNWASQIYAGIKVKQLCKLLRGTKALTDIV	
MUTATED AAS V E P R A E	T A
Q DESCRIPTION OF THE PROPERTY	UNI TEENELEI.EI EENIDET
İSÖLATE-E QPIELPEKDSWTVNDIQKLVGKLNWASQIYAGIKVKQLCKLLRGTKALTDIV	VPDIEEMEDELEENKEI
CONSTRUCT A OD 231 DEVENUMBAND TOVI MENT AND SOT VACT V2VOI.C21.1.PGAVAI.TDI	CV2LTEEAELELAENBET
CONSENSUS-A QP??LPEKDSWTVNDIQKLVGKLNWASQIYAGIK?KQLC?LLRGAKALTDI	
	тр -Т
	1 D
	/- D-S?E?
	-DA
	2-3222-22
CONSENSUS-CPZ -?I????P	
DESIGNED SEQ .LREPVHGVYYDPSKDLVAEVQKQGQDQWTYQIYQEPFKNLKTGKYSRKRSA	HTNDVROLTEVVOKIATE
MUTATED AAS K I I G F F(error) A M G	K AA V
	_
ISOLATE-E .LRIPVHGVYYDPSKDLVAEVQKQGQDQWTYQIYQEPFKNLKTGKYSRKRSAI	HTNDVRQLTEVVQKIATE
CONSENSUS-A . LK?PVHGVYYDP?KDLVAE?QKQGQDQWTYQIYQEPFKNLKTGKYA?KRSF	AHTNDVKQLTEVVQKV??E
CONSENSUS-Besiigrm-G-	Aiat-
ISOLATE-CEFSIINF-FFFFF	IAL-
CONSENSUS-DESIihGRm-G-	IsT-
CONSENSUS-OQ-DWV?I?-????EH?RQKAS	3IRA?SQ-
CONSENSUS-UESIIGQYRIK	AIAQ-
CONSENSUS-CPZ ???-???-???-?!???-????-?R????	???RA??I
	m=1 \/
	p51 \/
DESIGNED SEQ SIVIWGKTPKFRLPIQRETWETWWMEYWQATWIPEWEFVNTPPLVKLWYQLEK	DPIVGAETFIVDGAASK
MUTATED AAS K K A TD	E A V N
ISOLATE-E SIVIWGKTPKFRLPIQRETWETWWMEYWQATWIPEWEFVNTPPLVKLWYQLEK	THE THE A PERCENTAGE A SEC
ISOLATE-E SIVIWGKTPKFRLPIQRETWETWWMEYWQATWIPEWEFVNTPPLVKLWYQLEK	DI I VOIDILI I I DOILION
CONSENSUS-A SIVIWGK?PKFRLPIQ?ETWE?WWMEYWQATWIPEWEFVNTPPLVKLWYQLE	KDPI?GAETFYVDGAANR
CONSENSUS-BtkKtt	-ev
(SOLATE-CKKA-TD)	EA-V
CONSENSUS-DTKT?	-EI
CONSENSUS-O' ?-?L?VTRTA?SI??	?E?
ONSENSUS-UTKAT	TEV
CONSENSUS-CPZ????A?????????	
DESIGNED SEQ ETKLGKAGYVTDRGRQKVISLTETTNQKTELHAIHLALQDSGSEVNIVTDSQYF	
NUTATED AAS IV D Q Q L	r k r
TOOL MEDIA ON THE DESCRIPTION OF THE PROPERTY OF THE ALL ALL ALL ALL ALL ALL ALL ALL ALL AL	AT.GTTOAOPDRSESEVA
SOLATE-E ETKLGKAGYVTDRGRQKVISLTETTNQKTELHAIHLALQDSGSEVNIVTDSQYA	ADGIIQAQIDAGDOD V
ONSENSUS-A ETK?GKAGYVTDRGRQKVVSLTETTNQKTELHAIHLALQDSGSEVNIVTDSQY	ALGIIOAOPDRSESE?V
ONSENSUS-Bldql	k1-
SOLATE-CIIQQQ	LKT-
ONSENSUS-DLPf-DQ-NL	KL-
ONSENSUS-O ?LEQ-K-?IIK-?A-M-?L?KE?	??-SSTO-?-PI-
ONSENSUS-UKQQ	KI-
ONSENSUS-CPZ ????-??????QA?-?L??-???	·???-???L-
UNSENSUS-CEZ III	
ESIGNED SEQ SQIIEELIKKEKVYLSWVPAHKGIGGNEQVDKLVISGIRKVLFLDGINKAQEEH	IERYHSNWRTMASDFNL
UTATED AAS N K R A SA D	K NE
0	
SOLATE-E SQIIEELIKKEKVYLSWVPAHKGIGGNEQVDKLVISGIRKVLFLDGINKAQEEH	IERYHSNWRTMASDFNL
DNSENSUS-A NQIIEKLI?K?KVYLSWVPAHKGIGGNEQVDKLVS?GIRKVLFLDGIDKAQE?	HE?YH?NW?AMASDFNL
NNSENSUS-B	Ksr
SOLATE-CQS-ERE-	-KSRNEI
ONSENSUS-D sQK-EAE	KNR
	KSL?-G-
	KSR
ONSENSUS-UQQDE- ONSENSUS-CPZ ????K?E?I	-?S??-??? 5
)NSENSUS-CPZ ????K?E:1	-:::::
ESIGNED SEQ PPIVAKEIVANCDKCQLKGEAMHGQVDCSPGIWQLDCTHLEGKVILVAVHVASG	VTFAEVI PAETGOETA
	1 1 2 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1
JTATED AAS PS IN I	
C	

FIGURE 4 (Cont)

SUBSTITUTE SHEET (RULE 26)

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CONSENSUS-D CONSENSUS-O CONSENSUS-U CONSENSUS-CPZ	$egin{array}{llllllllllllllllllllllllllllllllllll$	CKSQ QHSQ K???? DIQTKELQKQITKIQNFRVYYRDSRDPI	D- 880 D- 798 E- 882 -?-D- 631
ISOLATE-E AEH	ILKTAVQMAVFIHNFKRKGGIGGYSAGERIIDIIAT	DIQTKELQKQITKIQNFRVYYRDSRDPI	WKGP
CONSENSUS-B ISOLATE-C CONSENSUS-D CONSENSUS-D CONSENSUS-O	HLKTAVQMAVFIHNFKRKGGIGGYSAGERIIDIIA 	tT	1 952 950 865 952
DESIGNED SEQ AKLI MUTATED AAS	vif cds -> LWKGEGAVVIQDNSDIKVVPRRKAKIIRDYGKQMAG	EDDCVAGRQDED A S	
ISOLATE-E AKLI	LWKGEGAVVIQDNSDIKVVPRRKAKIIRDYGKQMAG	DDCVAGRQDED .	
CONSENSUS-B	LLWKGEGAVVIQDNSDIKVVPRRKAKIIRDYGKQMA	V-s -	929 1002
CONSENSUS-D CONSENSUS-O -Q-	KGVV	V-S -T-SM-NT-SESMEQPGEIP VGKHGTAW	1000 925 1008 742
TOOTATE-C FROM GE	FROM LOS ALAMOS HIV SEQUENCE DATABASI ENBANK U46016 HIV-1 SUBTYPE C (ETHIO) ENBANK U51189 HIV-1 SUBTYPE E ISOLATI	PIA)	

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<- pol cds

DESTGNED SEO	MENRW.Q.VMIVWQV	DRMRIRT	WNSLVKHH	MYISKK	AKGWFYR	CHHYES	OHPKVSSEV	HIPLGEAR	FFAT	
MUTATED AAS	r	к	K	H	И	FD F	₹	D,	I	
ISOLATE-E	MENRW.Q.VMIVWQV	DRMRIRT	WNSLVKHH	MYISKK	AKQWFYR	HHYESO)HPKVSSEV	HIPLGEAR	LVI	
CONSENSUS-A	MENRW.Q.VMIVWQ	JDRMrIR'	TWNSLVKH	HMYVSKI	(AKGWFY	RHH£Es	RHpkvsSE	HIPLGdA	RLVV i	66 66
CONSENSUS-B	MENRW Q VLIVWQVI		K	т-д.	MCMAAL	HHYDSR	HPKVSSEVI	HIPLGE AR	rii .	-
ISOLATE-C			1/		・・・・・・・・・・・・・・・・・・・・・・・・・・・・・・・・・・・・・・・	xa-	D			65
CONSENSUS-D		0.077777	N V.	_ ヒヒ_ つ_ つ _	、つつバーウー・	V	-N-??-	· Y — ~ V ? ? –		54
CONSENSUS-O CONSENSUS-CP:	Z -3333.333	?		-I???-3	333-3-	Y??	33333-3	????????	K-?-	34
	RTYWGLQTGEKDWQLO	ייי די מנזימניי	ADONDAGE.	יינום מוניני	DOLTHI	OYFDCF	SDSTIRRA	LGQIVRRRC	EYP	
DESIGNED SEQ		-HGASTEN	L S	G	н І	H	A A	HR S	Q	
MUTATED AAs	K H R H	V	ĸ			Y				
•						_				
ISOLATE_E	RTYWGLQTGEKDWQLG									
CONSENSUS-A	RTYWGLHTGErDWHI	GhGVSIE	:WraKRYS]	OVDPDL	ADqLIHI	LhyfdC	FSdSAIRkA	ILGeiVRPR	CEYQ	136
CONSENSUS-A	•	. ~				- v ·	617	** 5		136
ISOLATE-C	THE PARTY OF THE P	けいつてきの アマかん	プロス・ロロマネアバ	バカロペガル	ригатимы	1 Y P LJC P	VERMIKVAT	TRIVADEVCT	J1Q	
CONSENSUS-D		^	VD		N	/Y	E:/	112:		132
CONSENSUS-O	m 140 777		_っぴ_り_ぴ_	_T_~ET	RM	1	-122		:	118 76
CONSENSUS-CPZ		?	?G?-?-	?T	???	???~.	-333-3-3-	222222-	K	76
				vnr	cds ->				•	
			•	-				•		
DECTONED SEO	SGHNKVGSLQYLAL.K	ALIT	PKKIRPPL	PSVKKL	TEDRWNK	CPQKIK	SHRENHTMN	GH		
UTATED AAS	A T	к	ĸ		K E	T	RG			
MUIAIED AAS										
SOLATE-E	SGHNKVGSLQYLAL.K	ALTT	PKRIRPPL	PSAKKT,	redrwnk	(PQKIK(SHRENPTMN	GH\$		
TOTAL TOTAL	AGHNKVGSLQYLAL.	LAT. V	aPtkaKPP	LPSvkKI	tEDRWn	ePQKTF	CGHRGsR?m	NgH\$		191
CONSENSUS-A		a i	t-k-i	?		K	(191
SOLATE-C	ACIMICATORIAN T	AT. TK	PKKAKPPI	PSVSKL	/EDKWNK	POKTRU	SKKGMAT T MM	Gn	•	
CONSENSUS-D	2	+ i	K-T	R		K				186
	25072	2-V	K????	Q?-		K???I-	DOP5-52-			161
CONSENSUS-O	;5Q1::		22222222	2222		K22R23	?-?EN?TR			107

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	;	/<-			olig	<- v omeriz	vif c zatio			->/		•	•	LR doma:	in
	DESIGNED SEQ MUTATED AAs	MEQ.	AP	EDQGPQRE SS	PYNE	WALELI T		QEAVRH H N	FPRPWLI	HNLG G S	H OATAE:	rygdt	WSGVEA E	LIRTLQQL I	
	ISOLATE-E	MEQ	AP :	EDQGPQRE	PYNE	WALELL	EELK	QEAVRH.	FPRPWLH	INLG	OYIYET	YGDT	VSGVEA:	LIRTLQQL	
	CONSENSUS-A CONSENSUS-B ISOLATE-C CONSENSUS-D CONSENSUS-O CONSENSUS-U CONSENSUS-CPZ	q? MEQ Q. Q.	AP I	EDQSSQRE	уи руие: уи- би- ни-	-Wt WTLELL -Wt -Wt	EELKN	?-A IEAVRHI S-A ?-A Q-A	PPRPWLH	-? IGLG(-S -a	E YIYNN -?E -YE	YGDTW	-aE- IEGVEAI -?E- E-	AIIRILQQL	6.
		:	LR d	omain ->	-/ t	at cds	s ->			,					
		LV		CQHSRIGI R CQHSRIGI	Ī T	RQRRA G RQRRA	s								
(CONSENSUS-A CONSENSUS-B ISOLATE-C	i-?	?	COHSRIG	-t		?								. 84 93
(CONSENSUS - D CONSENSUS - O CONSENSUS - U CONSENSUS - CPZ	I t	y	?-??	-t -???? -T	.RQA ?-rg: .RQA	S rS S	S S							93 94 96 54

```
3'sj
                                intramolecular
                                               3'sj
                               disulfide bonding
                                                \/
                                            | rev cds. ->/<- nls ->/
DESIGNED SEQ MDPVDPNLEPWNHPGSQPTTACSKCYCKKCCFHCQLCFLKKGLGISHGRKKR
                                                           KQRRGAPQSRKDHQYP
                              Т
                                       Y V T
                                                           R
                                                               R
                                                                   SE
                           K
                 к
                     К
MUTATED AAS
                               N
            MELVDPNLEPWNHPGSQPTTACSKCYCKKCCWHCQLCFLKKGLGISHGRKKR
                                                          KHRRGTPQSRKDHQYP
ISOLATE-E
            M?PVDPnLEPWnHPGSqPtTaCskCYCK?CCwHCqlCFLnKGLGISYGrKKR..r?RRgtPQs?kDhQnp
CONSENSUS-A
                                                                               64
            -e---r---k----k---tn---k--f---v--tt------..-Q--ra--dSqt--vs
                                                                              68
CONSENSUS-B
            65
CONSENSUS-C
                                                                              66
                                                                              68
                                                                              55
                                                                              68
                                                                              45
           exon \/ exon
DESIGNED SEQ IPEQPLPQTRGGNPTDPKESKKEVASKTETDPCD
                SPD GE KE A
MUTATED AAS
           IPEOPLPIIRGGNPTDPKESKKEVASKAETDPCD
ISOLATĖ-E
                                                                              95
            ipKQplPqtqg??ptgpkESkKkVeSKteTDrf?$
CONSENSUS-A
            Ls---?s-pr-D.----rE----P?d?
                                                                              99
CONSENSUS-B
            -s----p-D-
----ss-pR-d-----?---A---p-Dw$
                                                                              98
CONSENSUS-C
                                                                              99
CONSENSUS-D
            V----IS-AR-N.------E----A??-P?--$
                                                                              96
CONSENSUS-F
CONSENSUS-O V-?-S???-?RK.Q?RQE-QE??--K??GP?G?P????SC??CTR?S?Q$
CONSENSUS-U ---S--H--RV.S---E----A----D-
                                                                             83
                                                                             101
                                                                             52
CONSENSUS-CPZ ??-??-?????-.?????K??-?-??--?????-?
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				bindi	affinity ng site nls	<i>r</i>			
	\/ 3' sj	exon	<pre>\/ exon</pre>	/<-	-	·>/ [:]			
DESIGNED SEGMUTATED AAS	Q MAGRSGSTDE ELL D N	RAVRIINILYQ KI K	SNPYPSSEG	TROTRKNRR	RRWRARQF E	QIRAI:	SERIL W	STCLG NF	RS P
ISOLATE-E	MAGRSGSTDE ELL	RAVRIINILYQS	ENPYPSSEGO	TRQTRKNRRI	RRWRARQR	QIRAI	SERIL	STCLG	RS
CONSENSUS-A	MAgRSG?sDE.eLL								
CONSENSUS-B ISOLATE-C	MAGRSGDSDE ELL								
CONSENSUS-F	N-?T						-	_	•
CONSENSUS-O	EQ?-3								
CONSENSUS-U	DA								
CONSENSUS-CP	Z?E-???????-?	'?-VK	??-?-	.?-?R - ?-	333	5-5555	??-V-	5-55-	41
	Leu-rio	·h		• .					
	effector d								
		>/							
	•	•							
DESIGNED SEQ	AEPVPLQLPPLERLHL	DCSEDCGTSGT	QQSQGTETGV	GRPQISGES:	SVILGPGI	KN			
MUTATED AAs	N	SD		N L	AV S				
ISOLATE-E	TEPVPLQLPPLERLHL	DCSEDCGTSGT	QQSQGTETGV	_	SVILGPGT	KN			
CONSENSUS-A	AEPVPLQLPPlERLh								. 120
CONSENSUS-B	t	?	?-	sil	pe	E\$			115
ISOLATE-C	AEPVPLQLPPLERLNL)		
CONSENSUS-F	E??]								105
CONSENSUS-O	Q?NN?VDQ-?3								95
CONSENSUS-U	IC-							_	123
CONSENSUS-CPZ	PK-GD-EE-DK-S-	·Λ-Λ-Ι.Ι.Ο̈́́́́́́́́́́ΩΛ~~	SWISOPO-A	r-ETVPAGGN	1914-1			•	, 97

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env cds -> phos	phos
DESIGNED SEQ MTPL EIIAIVAFIVALIIAIVVWTIAYI EYRKLLRQR RIDRL IKRTRERA EDSGNES MUTATED AAS L L VF \underline{K} K E I	
CONSENSUS-A mtpL??? elcalvGLivaLiLalvvwTiVgI.eyKkllkqrKidrl?ikRireRA.EDSgNES CONSENSUS-B -qs- q-?a-v-a-if-?r-i-R	- 56 - 57 - 51 - 42
DESIGNED SEQ EGDTEE LSTM VDM GNYDLGVDNNL NUTATED AAS R AL	
CONSENSUS-A ?GDT?E.L?kLVEM.GnydlgvdnNL\$ CONSENSUS-B eqesa-?????-H?apwdvdD SOLATE-C DGDTEE LSTM VDM GNLRLLDVNDL	71 75
ONSENSUS-D EresaHhAPwd?Ddm- ONSENSUS-F EAEA?GPFIP-DI?	80 73 59
ONSENSUS-O N?EE-QEVM???SH-F?NPM.FE?? ONSENSUS-U DESTMYEYILDND ONSENSUS-ODFE22-222222222222FANP2.222DE	81 23

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<- vpU cds signal peptide / gpl20 *

		*	•		
, DESIGNED SEQ MUTATED AAs	MRVKETQMNWPNL WK R	W GTLILGLVIIC M M M	SA SD NLWVTVYYG E	VPVWRDADTTLFCAS E T	
CONSENSUS - A CONSENSUS - B CONSENSUS - C CONSENSUS - D CONSENSUS - E CONSENSUS - F CONSENSUS - G CONSENSUS - O CONSENSUS - U CONSENSUS - CP	Mrvmgiq?nyq?l.wr?? ??krkh-????r?r-w-qwir?-erh???Ket-m-wpnk?-R-M-R-W-HGK?-kr-W-Hkt-tMKaM?KrNr.Kl?-?E?-R-??-??	?lmlm ?LGFwmlm ?mLM llV 	vg.n	e-k E-t rd e-T ED	49 53 52 55 53 54 51 36
DESIGNED SEQ MUTATED AAs	DAKAHETEVHNVW ATHACVPTDP YD	VV	ם ע ע		
CONSENSUS-A CONSENSUS-B CONSENSUS-C CONSENSUS-D CONSENSUS-F CONSENSUS-G CONSENSUS-G CONSENSUS-O CONSENSUS-U	dAkAydtE?HNVW?aTHaCVPTD)		ddqv- lyd	E	113 119 117 121 120 120 114 91 56
	* *	***	•		
DESIGNED SEQ	PLCVTLNCTNANLINVN · F	HYPERVARIABLE REC	SIONS 1/2	•	
CONSENSUS - A CONSENSUS - B CONSENSUS - C CONSENSUS - D CONSENSUS - F CONSENSUS - G CONSENSUS - O CONSENSUS - U CONSENSUS - CPZ	PLCVTL?C.???????????????????????????????????	nv-i-nvsn t-?-?-q	iig-it	??????????????????????????????????????	126 133 132 131 150 139 143 129 105 60
	^*~ ^^~	ž.		•	
DESIGNED SEQ MUTATED AAs	HYPERVARIABLE R				
CONSENSUS-A CONSENSUS-B CONSENSUS-C CONSENSUS-E CONSENSUS-F CONSENSUS-G CONSENSUS-O CONSENSUS-U CONSENSUS-U	??eikNCsfNmTtelrd e??g-?????i-si?gmi?vdVr eP.gaQVn-??m-?-?V-V-k??-????-?-????	-ve-akpkq-hakQ?HakktE-AkpktE-Akp			160 169 166 165 185 177 182 164 137
e.					
DESIGNED SEQ MUTATED AAs	YRLINCNTSVIKQACPKVSFDPIPI S A T IT E	r N	NFNGTGPCKNVSSVQ0 K T T T	CTHG IKPVVSTQL R	

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		224
CONSENSUS-D		234 254
CONSENSUS-E	- WANNK	245
CONSENSUS-F CONSENSUS-G	m 7/	251
CONSENSUS-O		228
CONSENSUS-U		. 205 120
CONSENSUS-CP	Z -????T??-?-????D-?-?-?-?-	120
	<- V3 neutralization loop	
	^*^	
DESIGNED SEQ MUTATED AAS	LLNGSLAEE EIIIRSENLTNNAKTIIVHLNESVEINCTRP NNNTR K HYPERVARIABLE REGION VV F D V Q K V S T	N 3/4/5
	LLnGSLAe???v?irSenitnNaktiiVql??pV?InCtRP.nnntr.ks???vri???gpGq??afya.	279
CONSENSUS-A CONSENSUS-B		296
CONSENSUS-C		291 288
CONSENSUS-D		312
CONSENSUS-E	322 = 33====b.Neg-G	302
CONSENSUS-F CONSENSUS-G		305
CONSENSUS-H	n n.m.N	39 279
CONSENSUS-O	IT-Skg.kIr-Mgk?dsg-NT-N-?i-mt-eg-?-v.Qei?mW-S.	261
CONSENSUS-U CONSENSUS-CP2		. 142
	atralization loop ->	
	PROPERTY DESCRIPTION 2/4/E	
DESIGNED SEQ MUTATED AAs	HYPERVARIABLE REGION 3/4/5	
CONSENSUS-A	tgdiiG.dirqAhCnvsr?eWn?tlq?Va?qLr??f???nkt??iiF?n.ssGGD	320 342
CONSENSUS-B		. 334
CONSENSUS-C	-?-????i-?a?-kqk-gd?.lltkp	331
CONSENSUS-D	1	360
CONSENSUS-E CONSENSUS-F	- 'ACTES - 11	344
CONSENSUS-G		344 65
CONSENSUS-H	?-??-?-!??-?-?-?:??H????-P Ml???n?k???s-?-Y-?YnaTd-?ka-kqteRYLeLv?-????vtm?-n?s-?	321
CONSENSUS-O		306
CONSENSUS-U	?E???T-?-??N?T?-?-???-????-?????A-???-???-	157
CONDINGOS GEO] CD4 * . *^^^ ^^	
DECTONED SEC	HYPERVARIABLE REGION 3/4/5	
DESIGNED SEQ MUTATED AAS		
	lEitthsFnCggef?FYCnts?lF.nstW????????n?t.??????.??n?t???????sndtI	355
CONSENSUS-A		374
CONSENSUS-B CONSENSUS-C		366
CONSENSUS-D	p	361 398
CONSENSUS-E		372
CONSENSUS-F	m-nr	373
CONSENSUS-G		92
CONSENSUS-H		356
CONSENSUS-O		336 175
CONSENSUS-CPZ	P-V??-??????-??I	1/3
	* CD4 * ^^^	
DESIGNED SEQ MUTATED AAs	HYPERVARIABLE REGION 3/4/5	
	tlq.CrI.kqIvnm.wQrvgq.AmYapPIq.g?irb?sNITGllLTRDGg??nns??????	401
CONSENSUS-A		419
CONSENSUS-B CONSENSUS-C		411 405
CONSENSUS-D	p??ke?-s???	403

PIGURE 10 (Cont)

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	^^^		gp120 / gp41	
DESIGNED SEQ MUTATED AAS	TFRPGGGDIKDNWRSELYKYKVV I NMR	/KIEPLGVAPTR AKRRVV E K I K	EREKRA VG IGAMIFGFLO	ЗA
CONSENSUS - A CONSENSUS - B CONSENSUS - C CONSENSUS - C CONSENSUS - F CONSENSUS - G CONSENSUS - H CONSENSUS - O CONSENSUS - U CONSENSUS - U	•	-e-k??? -r		460 465 508 478 481 187 S- 462 435 ?- 227
DESIGNED SEQ MUTATED AAS	AGSTMGAASITLTVQARQLLSGIVQQ M L	·N <u>M</u>	1 22	
MUTATED AAS CONSENSUS-A CONSENSUS-B CONSENSUS-C CONSENSUS-D CONSENSUS-E CONSENSUS-F CONSENSUS-G CONSENSUS-O	AGSTmGAaSiTLTvQarqLlSGIVqq	-n	REISNYTNQIYE ILTESQNQC SL K KEISNYTNQIYE ILTESQNQC SL K KEISNYT?IIY? LIEESqnq cr-dl-t CR-dGl-s? RNq-e.ILT RNq-e.ILT RNq-n.l?- qq-n-vSS?-e.e-Q?A-?- RQV-G.L-D-K-	279 279 279 279 279 279 286 279 287 286 287 287 287 288 288 288
DESIGNED SEQ I	ORNEQELLELDKWASLWNWFDITNWLW KD A N SK	V I	1	-
CONSENSUS-F CONSENSUS-G CONSENSUS-O CONSENSUS-U CONSENSUS-CPZ	EKNEqdLLaLDkWanLwnWFdIsnWLVees	k	V	664 657 705 672 674 647 625
MUTATED AAS	LGR RG <u>G</u>	ns <u>n</u>	F V T R	

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```
q?E.agT-G-TG-g--.-e--p-Wtp-Pq---?-LYT---TII-Wt--L-SNLaSg.I...............qk
                                                                                       702
                                                                                       685
CONSENSUS-CPZ Q?-.?????E-?-?-.??--?-???-??-?----N-GIW--QS-TSLACN.V.W-##LKT---L
CONSENSUS-U
                                                                                       398
                                               <- rev cds
                            WEALKYL WNLLQYWGQELKISAVSLLNATAIAVAEGTDRVIEVAQRAGRAILHI
DESIGNED SEQ SLRGLRRG
MUTATED AAs
            slkglrlg.....weglkYb.wNLllyWgrELK?SAinLldtiAiavAgwtDRvIEigQrigRAilnI
?...??-...-a--w.--q-sq--n-vs--nat----Eg----vv--a?---h-
--r--qr-...-a---.Gs-vq--l---k---S
                                                                                       780
CONSENSUS-A
                                                                                       789
CONSENSUS-B
                                                                                       787
             ....R-....-a-----q--?q---n--S------Eg---?v--a?--v-h-
CONSENSUS-C
                                                                                       773
CONSENSUS-D
                                                                                       832
             CONSENSUS-E
                                                                                       787
CONSENSUS-F
                                                                                       800
CONSENSUS-G
                                                                                       767
CONSENSUS-O
                                                                                       741
CONSENSUS-CPZ I-HS---L.....R-R-CL-.GGIIQ---K---I---S---AT-----EG---I--AF-VTL-I-R--
                                                                                       460
DESIGNED SEQ PRRIRQGLERALL
MUTATED AAS
             T
                                                                                      793
             PrRIRQGlEraLl$
CONSENSUS-A
                                                                                      801
CONSENSUS-B -?----
                                                                                      800
CONSENSUS-C
                                                                                      785
             -------
CONSENSUS-D
                                                                                     . B45
CONSENSUS-E
                                                                                      798
CONSENSUS-F
                                                                                      813
CONSENSUS-G
                                                                                      779
CONSENSUS-O
                                                                                      754
CONSENSUS-U
                                                                                      473
CONSENSUS-CPZ -----
```

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TOTAL CEC	MGGKWSKSSLVGWPEVRERIE	COT	PPAAEGVGAVS	D LDKHGAIT	'SSNTPA
MUTATED AAS	C P A	RA	A AF	_	Α .
ISOLATE-E	MGGKWSKSSIVGWPQVRERIK		PPAAEGVGAVSQ		
CONSENSUS-A	MGGKWSKsSiVgWPeVrkRmR	qT	PEAAKGVGAvSQ	DLDkhGAiT	SSNt?? 4
CONSENSUS-B ISOLATE-C	?-?-??e	ra????????????????	Epd1 APAAEGVGAASR	D LDKYGALT:	SSNTPA
CONSENSUS-D	NT 77T.	~_ クラフラフ	dPDR		as 5 H-PO 3
CONSENSUS-O CONSENSUS-U	NA??-?KF???? ????????-E-I-	R?	-b3333	-33333-3-333	??A- 3
\vskip6pt	* SH3-binding	3 1 1 1	binding		
DESIGNED SEQ MUTATED AAs	NNADCVWLK AQE E EG	VGFPVRPQVPLRPMTYK	GAFDLSFFLKEK AV L	D I Q <u>D</u>	[LDFMA
ISOLATE-E		VGFPVRPQVPLRPMTYK			
CONSENSUS-A	tnpsCaWLE?Aqe?.de?.	VGFPVRPQVPLRPMTYK	gAvDLShFLKEK(GLDGLIYS?kRQEI	TLDLWV 110
CONSENSUS-B	npscawherager.der.	ZCERTID DOUBT D DMTVK	a-?KEKO	GLEGLIYSKKRQEI	:PDFMA
ISOLATE-C				EM-V	
CONSENSUS-D CONSENSUS-O	77 0 0777 2	? ? _ '	フードド	:	: 33
CONSENSUS-U	N-??-?????E?E.	?-	F?	??	83
\vskip6pt	•	SH3-bindi:	ng		
	•	*	2		· . ·
PEGICNED SEO	YHTQGFFPDWHNYTPGPGIRY	PLTFGWCFKLVPVDPRI	EVE EINKGENNC	LLHPMSQHGMEDEE	REVĻI
MUTATED AAs	и <u>Y</u> Q T	S	AE		
ISOLATE-E	YHTQGFFPDWHNYTPGPGIRY				
CONSENSUS-A	YnTQGfFPDWQNYTPGPGtRf.	PLTFGWCfKLVPvDPaH	VE.eat?GEnNS	LLHPICQHGMQDe:	? 174
CONSENSUS-B	YNTQGFFPDWQNTPGPGURY YNTQGFFPDWQNYTPGPGURY	DI.TECMCEKI.VPVDPSF	VE EINEGENNC	LLHPASLHGMEDEDI	REVLK
	~ T_V		EC-C		-dx 105
CONSENSUS-D	2 2 2	S?E-	A-RIGNT?-:A:	A-::E-:II.	1-: 100
CONSENSUS-U	-H???-?	???-?-	NC	?S?-?E	: 138
\vskip6pt		* .			
	THE PROPERTY OF THE PROPERTY O	VD <i>C</i>			•
DESIGNED SEQ MUTATED AAS	WKFDSRLARRHIARELRPEFY :	NDC .			•
		_			
ISOLATE-E	WKFDSALARRHIARELRPEFY :	KDC			
CONSENSUS-A	WkFDSrLAlkHrA?ElHPEfY.	KDC\$		Dar Dage	199 230
CONSENSUS-B	-rfh-m-ry	?TSMCLQGTFRWGI	SREARLGGTGEW:	KALIKCCI	230
	WKFDSHLARRHMARELHPEYY	KDC		•	206
	-R-NfE-K-R-m -?RS-G?T-???LF?			•	· - 166
CONSENSUS-O	S??-?-R-??-				157
こういつ ひいっこう			-		

GAG OVERLAPPING SEGMENTS

Segment 1	Segment 2	Segment 3	Segment 4	Segment 5	Segment 6
M G A R A S V L S G G K L D A W E K I R L R P G G K K Y (K) $(K$	WEKIRD R GGKKKYKMKHLVWASRELERFA RL tgg gag aaa atc aga ctg aga ccc gga ggc aaa aag aaa tac ara mtg aaa cac mtt gtg tgg gcc tcc agg gaa ctg gaa agg tjt gcc	M K H L V W A S R E L E R F A L N P G L L E T A E G C Q Q I L I mtg aag cat mtc gtc tgg gct agc aga gag ctc gag aga ttc gct ctg aat ccc rgc ctg ctc gag aca kcc gaa ggc tgt mag caa att	LNPGLLETAEGCQQILEEQLQSALKTGSEEL SKG PQCYC gcc ctc gaa acc kct gag gga tgt maa cag atc ctg gra cag ctc cag ycc gcc ctc mag aca ggc wcc gaa gag ctc	LEQLQSALKTGSEELKSLYNTIATLWCVHQ GPQcaa ctg caa yct gct ctg maa acc gga wca gag gaa ctg arg tcc ctg twt aac aca rtc gct acc ctc tgg tgt gtg cat cag	KSLYNTIATLWCVHQRIEVKDTKEALDKIE R F V ara agc ctc twc aat acc rtc gcc aca ctg tgg tgc gtc cac caa agg att gas gtc arg gac aca aag gaa gcc ctc gac aaa atc gaa

FIGURE 12 (Cont)

Segment 7	Segment 8	Segment 9		Segment 10		Segment 11	
RIEVKDTKEALDKIE EEQKKSQQKTQQAAAA DR aga atc gaw gtg ara gat acc aaa gag gct ctg gat aag att gag gag gwg caa aas aaa agc mag caa aag aca caa cag gct gcc gct	E Q K K S Q Q K T V N K	9 a cay aaw aay too maa cay aaa acc cay caa goo goo gat aca ggo arc too ago T G S S K V S Q N Y P I V Q N A Q G Q N N N N Q Q D N N D D N D D D D D D D	s acc gga art ago too maa gtg too cag aat tac oot ato gto cag aat syo caa ggo caa atg gto cac caa	Z	sc ttt	TLNAWVKVIEEKGFNPEVIPMFSALSEGAT V A S	aca ctg aat gcc tgg gtg aaa gtg rtt gag gaa aag gsa ttc art ccc gaa gtg att ccc atg ttt wcc gct ctg tcc gag gga gcc aca

Segment 12	Segment 13	Segment 14	Segment 15	Segment 16	Segment 17
PEVIPMFSALSEGATPQDLNMMLNIVGGHQHQ	P Q D L N M M L N I V G G H Q A A M Q M L K E T I N E E A A A C C cag gat ctc aac ayg atg ctg aat ayt gtg gga ggc cat cag gct atg caa atg ctg aaa gas aca atc aat gag gaa gcc gct	AAMQMLKETINEEAAEWDRVHPVHAGPIPPP	EWDRVHPVHAGPIPPGOMREPPRGSDIAGTT	GOMREPROSDIAGTTSTLOEQIGWMTNNPP	STLOEQIGWMTNNPPIPVGDIYKRWIILGL
T		D	I	I	
cct gag gtc atc cct atg ttc wca gcc ctc agc gaa ggc gct acc ccc caa gac ctg aat ayg atg ctc aac ayc gtc ggc gga cac caa		gct gcc atg cag atg ctc aag gaw acc att aac gaa gag gct gcc gag tgg gac aga rtc cat ccc gtc cat gcc gga ccc rtt scc cct	gaa tgg gat agg rtt cac cct gtg cac gct ggc cct rtc sct ccc ggc caa ats aga gag cct agg gga agc gat atc gct ggc aca acc	gga cag atr agg gaa ccc aga ggc tcc gac att gcc gga acc aca agc aca ctg caa gag caa atc gsa tgg atg aca arc aat ccc cct	. toc acc ctc cag gaa cag att gsc tgg atg aca art aac cct ccc rtc cct gtc gga gas att tac aaa agg tgg att atc ctc ggc ctg

			21	210	
Segment 18	Segment 19	Segment 20	Segment 21	Segment 22	Segment 23
I P V G D I Y K R W I I L G L N K I V R M Y Q P V S I L D I V C E E S S S S S S S S S S S S S S S S S	N K I V R M Y Q P V S I L D I R Q G P K E P F R D Y V D R F F R S S K A aat aag att gtc agg atg tac yma cct ctc tcc atc ctc gac att arg caa ggc cct aag gaa ccc ttt agg gat tac gtc gac aga ttc	RQGPKEPFRDYVDRFYKTLRAEQATOQFVKN K K SD ara cag gga ccc aaa gag cct ttc aga gac tat gtg gat agg ttt twc aaa acc ctc agg gct gag caa gcc wca cag gaw gtg aaa aac	Y K T L R A E Q A T Q E V K N W M T E T L L V Q N A N P D C F $ m K$ B $ m D$ T $ m K$ D $ m D$ twt aag aca ctg aga got we caa gas gte aag aat tgg atg ace gas aca ctg cte gtg caa aae get aae eet gae tgt	WMTETLLVQNANPDCKSILKALGTGATLEEE D tgg atg aca gaw acc ctc ctg gtc cag aat gcc aat ccc gat tgc aag wcc atc ctc arg gct ctg gga mcc gga gcc wca ctg gaa gag	KSILKALGTGATLEEMMTACOGVGGGPSHKA TRPS

Segment 29 Segment 27 gga aag 呂 Н α 出 又 Ø aac atc rtc <u>gg</u>c H >U Z \mathcal{O} \mathcal{Q} \bigcirc gct aat gaa ctg ttt cyc ď Н 口 口 z др ttt cag gyg amc mac cat mtc gct arg HZ 民 民民 站 弘 ہتا ഥ aac ccc gga aac 凶 ø Ö Z Z get QПH ď ∇ ď r gga cag aaa r 出 O ¥ Ø Дι taa ggc aga tgg aat ttc ara ggc aga **以** r Ŋ ⋈ 召 α gaa tgt gag \geq ĽΊ ഥ U 더 Ö 990 gat tgc.aca ď Z × \Box ¥ Н gag <u>3</u>80 gga aaa 闰 O Ö 又 \mathcal{O} N H S aga tgt aag taa 召 \mathcal{O} ď ¥ П Ŋ ctg gag ttt aac ада gg Ø \Box Z 召 区 Д atg aat cag atg aaa atc tgg \succeq \gt ഥ Д \mathbf{z} ⋈ tgc agg atg gcc $\mathbf{\Xi}$ α \mathcal{O} ď Q Н ggg atc aag agg cac ¥ ď Н 召 工 X rtc tgt gcc aat K Z H >U O r ดลด att aac gtc 口 ď Z 闰 П Hrgt mat ara ttc ス ara വ വ H Z 召 民民 ഥ amc ggg aat ដូ ggc HZ 노 ď Д Ċ Z gyc H L ggg Сmg tgt ∢ ⊳ C Ой C ď Caa aag Gad caa r Ø \Box 江 ¥ Q gtc agc arg tgg gga \triangleright 比 民 Ŋ CD \geq α atg ggc ttt tgc gag Ü \mathbf{z} ഥ \mathcal{O} 口 ഥ ggg caa aac ಡಡಿಡ acc Ø ď 区 z J Е tgc gaa tgt \mathcal{O} 闰 r t 区 J gct gcc agg tgc gac ď ď 召 U 凶 \Box ata. aat acc [--П \bigcirc Z 召 X atg ttc \triangleright Ξ ſΞţ Д \succeq atg tgt gct α Σ \mathcal{O} ď \bigcirc

⋈

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Segment 30 Segment 33 ttt ggc aat gac gat aag gag r 闰 \Box tto 呂 ഥ Z ttt rga **で** 足 r Д 呂 Γτι ഥ gcc agc ctc aag tcc ctg gaa arc \mathbb{Z} Оβ 口 gag 闰 Ŋ 闰 gcc caa Þ \bowtie Õ ggt 노 $\rho_{\mathbf{i}}$ Ц S P D gat acc ß Д ď വ ď acc CCC ccc cct tya \vdash E S Дι cct acc aca Д H Д \circ cct gag 团 \vdash Д വ H Y I L S L F G N D P L S age ctc ttc gga aac gat ccc tya gag gaa Д 闰 tcc arg 도 도 闰 gaa Ŋ ŋ 口 tte eyg cag tta aaa Oĭ Ē K rgg ДЪ \mathcal{O} Д ttc × ſτι 压 ggc aat $\overset{\text{art}}{\text{ort}}$ ΩЧ z Ċ 闰 团 Ŋ act cag gct tcc ctg aaa gct Д 戍 Õ ¥ ಇಇಇ ggg X α Д 口 act P O P \mathcal{O} Д ß agc 凶 ď ď Ŋ NHS act tya C H Д aga gag aca acc act acc വ Д E Д act 闰 Д \vdash Дι tgg Ч ⋈ 口 att 又 R R ara Н 口

POL OVERLAPPING SEGMENTS

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Segment 1	Segment 2	Segment 3	Segment 4	Segment 5	Segment 6
FFRENLAFQQGKAREFSSEQTGANSSASRK [T] PE P P R L P L Ltt agg gaa amc ctg gct ttc cmg caa ggc raa gcc aga gag ttt ycc agc gaa cag aca rga gcc aat agc ycc rcc tcc agg aaa	FSSEQTGANSSARKLGDGGGAERQGTSSSS P ttc yct tcc gag caa aca rgg gct aac tcc yct rca agc aga aag ctg gga gac gga gcc gas aga cag gga aca agc tcc agc	LGDGGGAERQGTSSFFPQITIWQRPLVT D ctc ggc gat ggc gg ggc ggc ga ggc acc tcc agc tcc ytc arc ttt ccc caa atc aca ctg tgg caa agg cct ctg gtc acc	FSFPQITLWQRPLVTIKIGGQLKEALLDTG LN ytt art ttc cct cag att acc ctc t9g cag aga ccc ctc gtg aca rtc aaa atc 9gc 9ga cag ctc awa 9a9 9ct ctg ctc 9ac aca 9gc	I K I G G Q L K E A L L D T G A D D T V L E D I N L P G K W V E aag att gga ggc caa ctg awa gaa gcc ctc ctg gat aca gga gcc gat gac acc gtc ctg gaa gaw ats aat ctg cct ggc arg tgg	ADDTVLEDINLPGKWKPKMIGGIGGFIKVR EM gct gac gat aca gtg otc gag gas ats aac ctc ccc gga ara tgg aag cct aag atg att ggc gga atc ggc gga ttc att aag qtg aga

	cot aag gto aag caa tgg cot ctg aca gag gaa aag att aag got ctg aca gmg att tgc ama gag gag yaa gag gga aag att agc
Segment 12	P K V K Q W P L T E E K I K A L T E I C K E M E E G K I S A T K
	cct atc gaw acc gtc cc gtc aag ctc aag cct ggc atg gac gga ccc aaa gtg aaa cag tgg ccc ctc acc gaa gag aaa atc aaa gcc
Segment 11	PIDTVPVKLKPGMDGPKVKQWPLTERKIKA E
	aat mtg ctc acc caa mtc gga ygc aca ctg aat ttc cct atc tcc ccc att gas aca gtg cct gtg aaa ctg aaa ccc gga atg gat ggc
Segment 10	NMLTQIGCTLNFPISPIDTVPVKLKPGMDG L R
	gga acc gtc otg gtc ggc ccc aca ccc gtc aac att atc gga agg aac mtg ctg aca cag mtt ggc ygc acc ctc aac ttt ccc att agc
Segment 9	LTQTG
	t att gag att tgc ggc
Segment 8	QYDQILIEICGKKAIGTVLVGPTPVNIIGR
	aaa ccc aaa atg atc gga ggc att gga ggc ttt atc aaa gtc agg cag tat gac caa atc mtt atc gaa atc tgt gga mas aag gct atc
Segment 7	KPKMIGGIGGFIKVRQYDQILIEICGKKAI

Segment 15

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26/216 Segment 16 Segment 17 gtg ttt agc gtc ccc ctc gac raa rrc $\Omega \cup \Omega$ aca 田区 <u>[-</u>; gtg \triangleright Д taa Ŋ П ಡಿಡಿರ ಇಡಿಡಿ ಇಡಿರ × Д ¥ \triangleright 又 Ŋ ಇಇಇ 凶 됴 gct tac gga ctg Ы \succ r K, gat gac Z, \Box Ω_{i} Ö cac 口 \triangleright cct gat Дι \Box atc ctg 니 gtc gga \mathcal{O} \triangleright age gte ace caa ctg Ц \vdash Ø > gtg \Rightarrow Ω gaa ಡಿಡಿದ್ದ ಇಡಿಡ 闰 凶 tgg Y ⋈ ttt ctc aag aaa ¥ ഥ gac K Д Õ Н <u>3</u>80 H \mathcal{O} gcc R ø. aag cat ccc X Д

FIGURE 12 (Cont)

gat ctg

agc

tat gtg gga

gat ctg

caa tac atg gac

gtg att tac

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aga

tta

ggg

Segment 19 Segment 20 Segment 22 Segment 21 atc ctc 口 ⋈ 口 口 aat gga tat cag Z Ċ Н , Oi \bigcirc cag cct agc aya aac maa Z K Q \bigcirc \succ r act MCC gtc atc ΗД HД \vdash Н tcc atg gtc ctg ß П ⋈ > 闰 gas atg Дı \gt വ Σ 口 atc ಇತ್ತದ tat aac Н Z 日日 Ŋ Д caa gct gct ttc aca \vdash Q Д ß ttc tat cag 压 \circ ഥ Z じ att X O R ď Н \triangleright agg SCC awa 1 tat acc H α ДД ⊱₁ att ggg agg × Н Д α 口 aga aag ggc tag tt 凶 ひ Ŋ 压 Д act gga cct 召 Ω_{i} Ç Д Д ttc gag ಇದದ aag 口。 Н X Ξ 더 gaa tgg Ω Ω Ω 闰 ≥ 口 \succ ggc raa 田式 Z r Н Ø gat 区 Omag ctc ccc caa Д z Ø Ŋ atg ayc П Д П HД Н act taa atg Д Ŋ Ц \succeq \triangleright gtg CCC gtg 5 Д \gt ⋈ S tac att 日 Gaw tac aat tcc Ŋ \vdash Z Ŋ ttc acc cag Ŀ H \succ \bigcirc tat ttt caa ttt × ĪΨ \circ ഥ gcc gcc tac Z, ď × Н gat aga aca $H \bowtie$ Д H K **点(日)** atc tac act \mathcal{O} \geq \vdash Ω_{i} 吆 aaa \triangleright ¥ C Ω 됴 agg CCC gga α Д r Д aca aaa П ഥ Н X 闰

FIGURE 12 (Cont)

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				28/2]	16	4	
Segment 23	Segment 24		Segment 25	Serment 26		Segment 27	
M D D L Y V G S D L E I G Q H R T K I E E L R A H L L R W G A E K	atg gat gac ctc tac gtc ggc tcc gac ctc gag att ggc caa cac agg rcc aaa atc gaa gag ctc agg sma cac ctc ctg ara tgg gga R T K I E E L R A H L L R W G F T T P D K K H Q K E P P F L (A) E K	Q a rca aag att gag gaa ctg aga smg	T T D	ttt acc aca ccc gat aag aaa cac caa aag gaa ccc cct ttc ctc tgg atg gga tac gaa ctg cat ccc gat agg tgg acc gtc cag cct	oc tgg aca gtg aat gac att	IELPEKDSWTVNDIQKLVGKLNWASQIYAG V P	att swg ctg cct gag aaa gaw agc tgg acc gtc aac gat atc caa aag ctc gtg gga aag ctc aac tgg gcc tcc cag att tac scc gga

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Segment 31 Segment 32 Segment 33	By a at agg gaa atc ctc ara gag cct gtg cat ggc gtc tac tac gat ccc tcc aag gat ctg rtc gct gaa rtc caa aag caa ggc $\frac{1}{1}$
Segment 32	PSKDLVAE $\overrightarrow{(V)}$ QKQGQDQWTYQIYQEPFKNI I G F FKN
Segment 31	NREILREPVHGVYYDPSKDLVAEVQKQG R aat agg gaa atc ctc ara gag cct gtg cat ggc gtc tac tac gat ccc tcc aag gat ctg rtc gct gaa rtc caa aag caa ggc
Segment 30	TDIVPLTEEAELELEERREETLREFVYYESTUREFVUHGVYESTUREFVUHGVYES SASSASSASSASSASSASSASSASSASSASSASSASSA
Segment 29	IKVKQLCKLLRGTKALTDIVPLTEEAELEL R att aag gtc ara cag ctc tgc aaa ctg ctc agg gga rca aag gct ctg aca gas att gtg mca ctg aca gag gaa gcc gaa ctg gaa ctg
Segment 28	K L V G K L N W A S Q I Y A G I K V K Q L C K L L R G T K A P R aaa ctg gtc ggc aaa ctg aat tgg gct agc caa atc tat sct ggc atc aaa gtg arg caa ctg tgt aag ctc ctg aga ggc rcc aaa gcc

Segment 34	Segment 35	Segment 36	Segment 37	Segment 38	Segment 39
L K T G K Y S R K R S A H T N D V R Q L T E V V Q K I A T E T E V V Q K $\overline{\text{L}}$ A T E T E V V Q K $\overline{\text{L}}$ A T $\overline{\text{L}}$ A T E V V Q K $\overline{\text{L}}$ A T E $$	DVRQLTEVVQKIATESIVIGKTPKFRLPI K AA gat ctg ara cag ctc acc gma gyc gtc cag aaa rtc gct acc gaa agc att gtg att tgg gga aag aca ccc aaa ttc ara ctg cct atc	SIVIWGKTPRPPIQRETWETWWMEYWOA K toc atc gtc atc tgg ggc aaa acc cct aag ttt arg ctc ccc att cag ara gag aca tgg gaa rcc tgg tgg ayg gas tat tgg caa gcc	QRETTWETWWMEYWQATWIPEWEFVNTPD. K	TWIPEWEPUNTPPLVKLWYQLEKDPIVGA $\mathbb R$ RUYQLEKDPIVGA $\mathbb R$ Ruyque $\mathbb R$ Ruyque $\mathbb R$ Ruyque $\mathbb R$ Ruyque aca ccc cct ctg gtc aag ctc tgg tat cag ctc gag aaa gas cct atc gyt ggc gyt gag	K L W Y Q L E K D P I V G A E T F Y V D G A A S R E T K L G A L B Y L G A L B R E T K L G A L B R E T K L G A L B R E T K L G A L B R E T K L G A L B R E T K L G A L B R E T K L G A L B R E T K L G A R E T K L G E A R E T K L G E A R E T K L G E A R E T K L G E A R E T K L G E A R E T K L G E E T K L G E A R E T K L G E A R E T K L G E E T C E T E T K L G E E T K L G E E T C E T E T C E T E T C E T E T C E T E T

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Segment 45 gac ara ago Ŋ K r 民民 凶 Н atc Н Ċ Д act gtc Д Ц N atc att cwg gct cag 田 Ø ď 口 ď ОΊ Н Д att \triangleright Н \vdash cag ò ⊠ \vdash art gga r SS A gtg ctg П \triangleright Ы gct stc Þ Ь Ч × gag tac \triangleright ⋈ 闰 Caa tcc \bigcirc Ŋ agc gag ß 闰 工 gat tac 区 Ŋ Д acc arg K S [--1 民民 gta gat \gt \Box Н atc CCC Н Н Дι caa 田瓦区 \circ Z gtg gcc \triangleright ø 闰 cwa gaa 闰 ЦЮ Н C tyg tyg atc Н Н att gga ტ Õ \vdash ggc S Z ß r gat ctc 口 \gt Д gcc ∢ \bigcirc tat П \succ 闰 ď Q Ω

FIGURE 12 (Cont)

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Segment 56 Segment 53 Segment 54 atc gtc 990 gct agc caa K Ç ď Ö gag gac aat aag rtt 闰 П Z ⋈ Ŋ gct L ntc tgg atc cct tac aat ccc caa ⋈ O ⋖ Д ttt gag aca gcc ,tgc gga \mathbf{C} 団 ſΞı \vdash α cac tac gag 口 ď Z Н \bowtie gct gct tac ara ryc att cac ctc ø Н Þ Ы ⊱∹ ggc acc aag ¥ \mathcal{O} Н \triangleright Д gaa gtc aca tcc K \gt Ŋ ഥ Н tgc gcc cag gtg K H ď Q \triangleright \mathcal{O} rct gat gtc ttc gga ggt \gt r ď Д ഥ ctg tgg 闰 出 \vdash ⋈ S caa gtc gaa ಇದಿ aga Ø \triangleright ĮΉ 足 \vdash ttc t39 gcc gca ggc ス O maa Ç Ø ď ഥ att gct aat gct \triangleright Д ď Z Н 980 ctg ctg agc atc gcc rrt z v Ы \vdash 口 Ŋ gtg gga CCC × r ⋖ Н \triangleright rtc gaa ctg aac tgg tac \triangleright 闰 П Z ⋈ ggg mtt gat tgg 凶 Þ Д Н Д ⋈ $\stackrel{N}{\mathrm{rat}}$ gaa ಇ೦೦ tgt <u>3</u>gc たなな ט ഥ Е \mathcal{O} 闰 tat cat gtg atc gaa gcc gct 口 ď 口 \vdash \triangleright tat gcc Caa ctg atc Н ⋖ Н \succ ď aaa ggc cat gga rya $\supset \Box$ K 耳 Ü \vdash gag 又 R arg cat ಇದ್ agc \triangleright \vdash Ŋ 闰 A A T T T recerted ats tgt gct gtc caa U \triangleright ℧ O gtg ggg Д \Box \gt Ç cat gaa ctc tgg tcc П 出 ⊠ വ Н gtg agg \bigcirc \triangleright α \vdash 囯 ttt tgg gct gga aaa ∢ ⋈ ø Ö ഥ ctg gtg gca CCC Н \triangleright Д ø, Z ctc 口 \mathcal{O} $\boldsymbol{\vdash}$ Ŋ \vdash

Segment 57	Segment 58	Segment 59	Segment 60	Segment 61	Segment 62
N I K Q E F G I P Y N P Q S Q G V V E S M N K E L K K I I G G Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q	G V V E S M N K E L K K I I G Q V R E Q A E H L K T A V Q M D D gag gtc gag tcc atg aat aag gaa ctg aaa aag att atc gga cag gtc agg gam cag gct gag cat ctg aaa acc gct gtg caa atg	QVREQAEHLKTAVQMAVFIHNFKRGGIGGG D caa gtg aga gas caa gcc gaa cac ctc aag aca gcc gtc cag atg gcc gtc ttc att cac aat ttc aaa agg ara ggc gga atc gga ggc	A V F I H N F K R K G G I G G Y S A G E R I I D I I A T D I (R) (R) S A G E R I I D I I A S D I S get gfg ttt atc cat aac ttt aag aga arg gga agt att ggc gga tac tcc gcc gga gag aga atc rtt gac att atc gct asc gat atc	YSAGERIIDIIATDIQTKELQKQITKIQUKQITKIQNF V tat agc gct ggc gaa agg att rtc gat atc att gcc wcc gac att cag tat aag gaa ctg caa aas caa atc mya aag att cag aat ttc	Q T K E L Q K Q I T K I Q N F R V Y Y R D S R D P I W K G P N F R V Y Y R D S R D P I W K G P L L L Caa tac aaa gag ctc cag aam cag att myc aaa atc caa aac ttt agg gtc tac tat agg gat agc aga gac cct mtc tgg aag gga ccc

FIGURE 12 (Cont)

Segment 65 C V A G
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tgt gtg gct rgc gtc atc caa gac gtc gtg cct agg aga aag gct aag att atc П Q \bowtie Н \mathbf{c} ¢ \gt G K Q M A G D D (A gga aag caa atg gct ggc gmt gac gtg K \triangleright ggc gct 凶 ď പ്പ Ċ gaa വ 뙤 ggc Ç \triangleright 又 att cag gat aac tcc gac att aag K ⋈ ctc 口 ctg tac Д × Н gat aaa വ 凶 Д ggg gcc aaa atc att agg z ∢ α cct Д Д Н gga Õ \mathcal{O} \vdash 뇌 Н ¥ tgg gtg \triangleright ⋈ ø H L H gtc \triangleright 呂 gg gcc ď Д α gat gga r Д 召 E gag atc aaa gtg gtc ccc tcc agg 斘 Д gga r Ŋ \triangleright gac aag ¥ \triangleright tgg ≊ 民 뇌 tac . П ⊱ Н tat gat $^{\rm ct}_{\rm ct}$ Д aag ¥ ß aat gat ď 吆 Z

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gas gct arg tac agc cra O R ß α atc Н വ \succeq yac gaw gat agg 田口 召 ĭ K Ċ two two ☐ \mathbf{Z} 口 gag cac cat > 出 出 Д gaa gat O 口 冮 Н ¥ α 耳 ⋈ tac gta gta \triangleright \triangleright × \triangleright ttt atc Н 口 ഥ 闰 $\underline{\Gamma}_{\text{mtg}}$ acc tgg Σ Ŋ ⋈ ß N aas gtg r \triangleright വ aas caa M Z Õ × \triangleright gct tgg ø ⋈ Н 又 X Д α α ಡಿಡಿಡಿ 区 江 Z O'R S 民民 ഗ 闰 att ⋈ Н വ \succeq

VIF OVERLAPPING SEGMENTS

tgg agg gag ggc gtc agc att Qgaw 990 cas ОĦ 区区 acc ctg caw ؤ 克 도 rtt rtt H D Maw

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Segment 8 Segment 7 gat cas agc rca atc Ŋ \vdash \succ \Box gaa Þ Д $\vdash \triangleleft$ 口 Д ggg tga ggc tcc ctg caa tac ctc Ø \mathcal{O} Ы ß П gat Н \succ Д 召 act gra tgc ttt kcc D U $\Sigma \triangleleft$ വ് Ø Д വ വ Д. 民民 Дι ഥ gac gtg Ŋ \mathcal{O} П \triangleright gat gtc aka \triangleright ΗЩ Ç 区 Д gtc gag Cas X OH \triangleright Ø ᇤ aag agc aca 凶 Д r \vdash \bowtie cac aat ctg \bigcirc Ξ Z S Ц tat ata att 耳 Ŋ Н Н Ц cac СD 及ら 口 ď П $\alpha \leq \frac{1}{2}$ ¥ 吆 ď Ф С С П С П С M T O X H П 叫 tat att Caw 口 召 OH Н \bowtie rcc gag gac \bowtie 闰 ď \geq Д taa gaa gat tgt ಠ വ \mathbf{c} Д 뙤 gac atc ⊱ Ы Д 足 \vdash kct tcc 召 Q D U S A Ŋ tto R Sgg agg gtg \triangleright Д দ 口 tgt U Ċ \Box Ŋ gtg cas gac 日民 び赶 \triangleright \Box Ç Caw ⊞ ⊗ ttt C Õ 땓 \triangleright tac ctg ggc \succ 口 \vdash r × taa ctc Caw ŎЖ ß OH X П z tgg П 耳 ≥ \bowtie Н gat gct cat Ç \Box 及ら 工 ď α 以及 ¥ \vdash α дΩ MID 口 α 闰

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FIGURE 12 (Cont)

Segment 12 cct ccc ctc ccc tcc gtg aaa aag ctc acc gaa gac ara tgg aat rag cct caa aag aya HH Q K I K G H R E N H T M N G H
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VPR OVERLAPPING SEGMENTS

39/216

Segment 1	Segment 2	Segment 3	Segment 4
MEQAPEDQGPQREPYNEWALELLEELKQEA	gaa cag gct ccc gaa gac caa rgc yct	aac gaa tgg rca ctg gaa ctg ctc gag gaa ctg aaa maw gaa gcc gtg aga cac ttt ccc aga ccc tgg ctg cat rrc ctc ggc caa yac VRHFPPRPWLHNLGQYITYETYGDTWEB GH S S gtc agg cat ttc cct agg ctc cac rrc ctg gga cag yac atc tat gag aca tac gga gac aca tgg kmg gga gtg gaa gcc ctc	IYETYGDTW(S)GVEALIRTLQQLMFIHFRIG
SS T	E W A L E L L E E E		E

FIGURE 12 (Cont)

att tac gaa acc tat ggc gat acc tgg kma ggc gtc gag gct ctg atc aga ayc ctc cag caa ctg mtg ttt rtc cat ttc aga atc gga

FIGURE 12 (Cont)

att agg ayc ctg caa cag ctc mtg ttc rtt cac ttt agg att ggc tgc crg cac tcc agg att ggc att myc aga cag aga agg gsc aga \triangleleft വ് വ് Õ **ДНЕ** Ŋ α ល \triangleleft \bowtie O \mathcal{Q} Z α \triangleleft 召 α O_{i} H >召 HHH Z I \vdash \Box Н 民 വ \vdash 田 O R \mathcal{O}

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Segment 6

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Segment 1		Segment 2		Segment 3	Segment 4	Segment 5
MELVDPNLEPWNHPGSQPTTACSKCYCKKC DP K K K	atg gaw cyc gtc gac oct aas otc gag oct tgg aaw cac oct ggc toc cag oct amg aca goc tgt wmc aaa tgc tat tgc aaa aag tgc	S Q P T T A C S K C Y C K K C C F H C Q L C F L K K G L G I K T	m N agc caa ccc ama acc gct tgc wmc aag tgt tac tgt aag aaa tgt tgc twc cac tgt cag stc tgc ttc ctg ama aag gga ctg gga atc	CFHCQLCFKGFLG TSHGRKKRGGRPQ Y tgt twt cat tgc caa stg tgt ttt ctc amg aaa ggc ctc ggc att agc yac gga agg aaa aag aga aga aga aga aga a	HGRKKR (\overline{K}) QRRGAPQSR (\overline{K}) DHQYPIPEQI	S R 🔘 D H Q Y P I P E Q P L P Q T R G G N P T D P K E S K K S S P D G S S E toc ags cag gar cat cag tat ccc att ycc gaa cag cct ctg yct cag mca agg gga grc aat ccc aca grc cct rag gaa agc aaa aag

TAT OVERLAPPING SEGMENTS

Segment 6

QTRGGNPTDPKESKKEVASKTETDPCDPCDPCDPCDPCDPcaa mcc aga ggc grt aac cct acc grt ccc raa gag tcc aag aca gac cct tkt gac

Segment 2 att ctg act was caa ctg ນ ⊟ ⋈ 口 口 Õ Д α Н tcc aac cct tac ate cre kee ate tee gag wgg ctg 区 区 П \succ 民 cct Д 团 α Д 召 \triangleright Z Ŋ gat Ŋ z Д Н tat cag arg 比 民 K S Õ 闰 gct 民田 × വ് Þ atc att aas att ctg aga ycc വെ Н Н caa Н Õ 民 Ø caa agg വ് Z X α \mathcal{O} G T F S ggc wcc Н Õ Ы agc amc tkc CH \mathcal{O} 召 \vdash rtc aga A Eff i z 召 闰 ß \triangleright \vdash 召 ß О О П 233 tgg ctc gct ď ⋈ 口 agg 民民 Н 召 ctg tat aga П 召 Z X \succ นนน gaa П Д വ് 口 gag agc aat aga 口 z വ് Ŋ ಇಇದ gaa വ Z Н [노] caa 环 克 gra gra Kot kot Ø \Box tac agg R H ctt വ് \succ \vdash ₽ ₽ H rrc gta SDZ Ы Н atc cag cag gga Н r Ø Õ N aaw 召 召 Ŋ atc S MCa Ø 召 · |--| aga Ç C Н ט 足 R Sma ¢ 召 口 rt H aga Ξ Ŋ 民

REV OVERLAPPING SEGMENTS

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FIGURE 12 (Cont)

Segment 6 EDCGTSGTQQSQTTTGVGSQGTTTGVGS att tyg gga gag tcc agc gyt rtc ctc ggc ycc gga r Di W С 口 \forall ß Ω 闰 Ŋ E O Н Õ R P S S mrc cat \mathcal{Q} acc ggc gtc \triangleright Ö Н gat tgc tcc 闰 Ŋ \mathcal{O} Н Д r H L . N mac ctg tcc cag Õ ß cag aga ctg Д Õ ೧೩೩ 呂 Õ gag 闰 \vdash aca ata \mathcal{O} П Д ß cct \vdash Д

VPU OVERLAPPING SEGMENTS

45/216

Segment 1	Segment 2	Segment 3	Segment 4	Segment 5
MTPLEIIAIVAFIVALIIAIVEYIEY at TALTARIA TON TIFY TEY LOOP See at get at get get to get at get get to get at get get get get get get at get at get get get at get get get get at get get at get get get at get get get get get get get get get ge	LIIAIVVWTIAYIEYRKLLRQRRIDDRLIKR	RKLLRQRRIDRLIKRTRERAEDSGNESED	TRERRAEDSGNESEGDTEELSTMVDMGNYDL	TEELLSTMVDMGNYDLGVDNNL
	L	(K) K K	I	R
	ctg att mtc gct atc gtg tgg acc att gyg twt atc gaa tac arg aaa ctg ctc arg caa agg ara atc gat agg ctc atc raa agg	ara aag ctc ctg ara cag aga arg att gac aga ctg att rag aga ayc aga gag aga gcc gaa gac tcc ggc aat gag tcc gag gga gac	aya agg gaa agg gct gag gat agc gga aac gaa agc gaa agc gat asa gaa gag ctc agc rca wtg gtc gac atg ggc aat tac gat ctg	asa gag gaa ctg tcc rcc wtg gtg gat atg gga aac tat gac ctc ggc gtc gac aat aac ctc

FIGURE 12 (Cont)

ENV OVERLAPPING SEGMENTS

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Segment 1	Segment 2	Segment 3	Segment 4	Segment 5	Segment 6
M R V K E T Q M N W P N L W K W G T L I L G L V I I C S A S . R M M M M atg aga gra aaa gag aca cag atg aac tgg ccc aat ctg tgg axg tgg ggc aca mtg att ctg gga mtg gtc ats att tgc tcc gcc tcc	W G T L I L G L V I I C S A S D N L W V T V Y Y G V P V W R M Egg gga acc wtg atc ctc ggc wtg gtg atk atc tgt agc gct agc gas aat ctg tgg gtg aca gtg tat tac gga gtg cct gtg tgg agg	DNLWVTVYYGVPVWRDADTTLFCASDAKAH E gam aac oto tgg gtc acc gtc tac tat ggc gtc ccc gtc tgg aga gas gct rmc aca acc oto ttc tgt gcc tcc gac gct aag gct yac	DADTTLFCASDAKAHETEVHNVWATHRACVP ET gam gcc xmt acc aca ctg ttt tgc gct agc gat gcc aaa gcc yat gas aca gag gtc cac aat gtg tgg gcc aca cac gct tgc gtc ccc	臣 T E V H N V W A T H A C V P T D P N P Q E I H L E N V T E D D N P Q E I H L E N V T E D D N P Q E I H L E N V T E D D N P Q E I H L E N V T E D D N D Sam acc gaa gtg cat aac gtc tgg gct acc cat gcc tgt gtg cct acc gat ccc aat ccc caa gag rtt swc ctc gag aat gtg aca gag	TDPNPQEIHLENVTENPMWKNNMVEQEO VV aca gac cct aac cct cag gaa rtc swt ctg gaa aac gtc acc gaa aac ttt aac atg tgg aaa aac rat atg gtc gas caa atg caw gag

Segment 9

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TIGHTRE 12 (Cont.)

Segment 7 ate tee etg tgg gae caa age ete aag eet tge gte aag gtg aaa otg aca ccc ctc tgc gtc acc ctc aac tgt acc aat gcc aat ctg ¥ П > z ט ď Д Z 凶 \vdash Н \mathbf{c} z Ŋ 니 Ø Д Н ≥ \triangleright Н ט Ŋ П Н Д T n gaa gac rtt a \gt Д П 闰 凶 Cam Cam > D E gat cag tcc ctg aaa ccc tgt Σ \mathcal{O} Õ Д 团 × gtg ᆸ \triangleright N N M V D D aat rac atg g Ŋ Ø Д tgg aag agc ctc tgg ĸ ⋈ 니 ⋈ ttc aat atg Σ ß att z اعتا aat gat Z \Box

L T P L C V T L N C T N A N L I N V N at a c ac cct ct g tgt gtg aca ctg aat tgc aca aac gct aac ctc atc aat gtg aat

GAP IN SEGMENTS DUE TO HYPERVARIABLE REGIONS 1 AND 2

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Segment 1	Segment 2	Segment 3	Segment 4	Segment 5
Y R L I N C N T S V I K Q A C P K V S F D P I P I H Y C $\overline{\Pi}$ P S R L S F D P I B I H Y C $\overline{\Pi}$ P S S A T I T E A T A T A T A T A T A T A T A T A T	KVSFDPIP ITE	aaa rtc wcc ttc gam ccc att ccc att cac tat tgc rct ccc gcc gga twc gct G Y A I L K C N D K N F N G T G P C F	got ggo twt gcc att ctg aaa tgc aat rac aaa ams ttt aac gga acc tgt amg aat gtg tcc asc gtc cag tgt acc cat ggc T G P C K N V S S V Q C T H G I K P V V S T Q L L L N G S L T $^{\circ}$ T T R aca ggc cct tgc ama aac gtc agc wac gtg caa tgc aca cac gga atc ara ccc gtc gtg tcc acc caa ctg ctc ctg aat ggc tcc ctg	IKPVVSTQLLLNGSLAEEEIIIRSENLTNN V att arg cct gtg gtc agc aca cag ctc ctg ctc aac gga agc ctc gcc gaa gag gaa rtc rtt atc aga agc gaa aac ytt acc rat aac

FIGURE 12 (Cont)

Segment 6 Segment 7 N L T N N A K T I I V H L N E S V E I N F F D V Q K V aca rac aat gyc aaa acc att atc gtc cam ctc aac raa agc gtc gwg att aac gag E K E 团 I I V H L N E \bigcirc X atc att gtg caw ctg aat ra att agg tcc വ 凶 闰 闰 H 闰 ď

Segment 5 ctg gga rtc gct gcc g α ď ď. \Box \geq ctg ಇಇಇ Caa ctc cag ctc acc gtc r K ₫ Q 口 \gt ggc caa cag arc aat Щ 闰 U \triangleright Z E 召 口 Н S N Д Ы នឧថ្ម 区 区 Õ Q 闰 ഥ Н gta П U \triangleright \vdash Õ rag gtg atg wtt ytc tcc ats gtc cag cat mtg r 다 \triangleright Q K $H \Sigma$ ΗБ \triangleright 口 \triangleright 民 ഗ gtc ggg caa cag 召 Õ \geq ⋈ ď Н gct aag gct gga 凶 区 ď K. Ç Õ tat 990 ggc gaa ď r \Box Ŋ ø aag ggc mtt ctc ara 뇌 民区 Н П \succeq 口 口 acc acc atg tat \succ \vdash r Н 니 ctg gtc ggt tac gct agg cwa Вη Ы Д \triangleright Ŋ ď 990 ď 民 闰 ď r 凶 rttgct Ŋ \triangleright 民 ℧ ಠ 口 cag \mathcal{O} K ď Ø П 召 gtc aac CtC \triangleright ⋈ П 闰 \mathcal{O} Z acc ctc acc CCC caa art z Д പ്പ Ц Н Sgac 日内元 Esaa Saa ttt Õ Д ĪΉ Ы gtg cag 区区 ⊟ r O Н agc atk ats 内 Haa ⋈ HΣ μД O wta rat gta agg att gtg HI \Box ß \triangleright 召 atg gct ggc gtg aga r \triangleright 召 \succeq ď \vdash aaa aag gcc gcc gga X 呂 r ď r ⋖ tac gct gga Ø \mathcal{O} \succ O Ç Ŋ I III III atg aaa ¥ α Д ⋈ П tac а С а С В Ы 召 \succ Е Н ctc ഥ 口 വ ΝП Д \triangleright ayc H gct പ്പ 闰 ď ď \mathcal{O}

GAP IN SEGMENTS DUE TO HYPERVARIABLE REGIONS 3,4 AND

FIGURE 12 (Cont)

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agg aat gag maa gas

gat

cag

aac caa

caa

gaa

ctc

tac

GWG

acc

tat

aac

tac

atc

gaa

Segment 10 Segment 11 Segment 9 att ctg tcc aac K Z \succ Z Ы \Box aga gga ats saa П Ç Ŋ Н α 田〇日 rag gag agc tgg 口 വ Z 田区 日日 $\Sigma \vdash$ rtt tgt tat aac agc wcc O M \mathcal{O} $\Omega \vdash$ ⋈ \succ \triangleright ggg ಇ೦೦ atc Þ Ö Ø Н Н 闰 CWA ОЧ Ц ≊ Z ⋈ Z gtg tgg mtc aac arc \bowtie \bowtie \gt \neg ⋈ z α aga act ಇದಿ gga rat r 召 Д ZQ Е А ggg tac . ctg gtg П \triangleright ≥ ď ⋈ Õ KFI QL aat ೧ಇಇ acc rmt K Z Ø Z Õ \mathbf{H} ctg gag aga 口 ⊟ 闰 വ Z aca att caa ตลล gaa Н Õ Õ ഥ O \vdash gag aag gac tga ytc \mathcal{O} X Д 디디 口 Ŋ I I (L att aaa tac M Ø വ് Ή Н <u>3</u>3c ctg Ċ П 又 团 \vdash tat ಕ್ರತ್ತ aaa aat tgg ≥ \succ 뇌 Z ⋈ 口 gtg ggc Eag Sag \triangleright 召 r Ŋ Н tac tgg ಇದಿ gaa atk Н 臼 Ŋ ⋈ Z H 田区 rtc ลรด tga tgg C $\Omega \vdash$ ⋈ Ы gat gga gaa tcc ಇದಿ Q Þ Ö Ω Н ctg ctg tgg aat atg 口 Ы ≥ Z ⋈ Owtg gtc H L μZ Z \mathbb{Z} \triangleright ≊ rac Cac agg ដូ ggc ტ Z A 口 异 Д \vdash gct tgg 口 O ď \triangleright ≥ \succ cag atc cag 光口中 KING Q Z A Ø \vdash z gat ctc gaa ₩ O M K, 口 H 口 ഗ gag cag 闰 Q Q \vdash 国 Н aaa gat tgt ytt 又 \mathbf{C} H H Н П 闰 atc atc agc 노 ď Н വ 召 gga ctc ಇಇಇ C α Н K 闰

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Segment 15 Segment 16 Segment 14 Segment 17 myc gag tcc atc rtt aac ggc H \vdash \Box ט Z 口 Ö ctc gga ttt rac att gaa ctc gtg art П \triangleright \vdash U 闰 S Z gtg gag Н \vdash Д \triangleright 团 \triangleright Caa att att Н 压 Н Ω Q П tgg အရှင gtc agg att atg gcc gtc ctg tcc ttc CD PK ⋈ ⋈ Н Гъ 召 aat gra 田は z Н \triangleright \triangleright Ω ttc tgg ctg cyc agc ď ць ⋈ Гъ Ŋ П ctc ttt cct att aga aga Ц \vdash لترا Д 召 പ്പ gra att rtc agc gac K \triangleright \vdash D U Ŋ വ Д gct tat act 召 ø \vdash Н \succ Д 380 tac agg tgg G G ggc ⋈ α Ö r \succ tgg ctc aaa caa aga O R 又 ႕ ⋈ Ø 区 gac gga gg Н r 召 Д 闰 rttgtc gct tgg \vdash П ⊠ \triangleright ď r gmg ลลธ ctg agg ggg 囯 Z X Д 足 Д r шyg gga aat cta E S 니 日 Ы Ċ Z 闰 ggc ctg rta ctg П Н Н r \triangleright 口 gam rat gtc ಇದಡ att 口 A Z \triangleright Н Н 闰 ttc cag mag ಇತ್ತಿದ O X ᇿ Ø Н Ŋ tgg atg ctc ttt gaa 闰 ≥ \mathcal{D} \mathbf{z} \Box بتإ atc aac gtg aga aac Z Н EI C Z \triangleright Ŋ tgg ttt gct ata cyg ⊠ дη α Ø П ĪΉ gac ctg ttc atc CCC agg 口 Д Hഥ Д α rtt < tac tac gat caa aaa Õ Ŋ ¥ വ Д cag gaa atc tac ggg Ø ಠ Н Н >Д tgg tat gga \geq Z Ы 內 r \mathcal{O} tgg cag K П Õ ⋈ Õ α tcc gat aga cct Ŋ C Д 口 α Д ctg tgg 闰 口 3 Н \triangleright Þ a K Z ggt 田口口 aga 口 Н വ് Д

Segment 22 gcc r r ഥ ď \circ ctc tgg aca aga 民 ⋈ 口 召 Н ⋖ ggg R Q Gra ggg tat \mathcal{O} Ճ \succ ⋖ \triangleright aga arc ctc gyt ctc Сма aat Н 口 < > ВΩ 団 Z ctg atc ctc ctg Ŋ Z Ç П 口 Н ctg ara 民民 口 П 召 \vdash \gt ctg atc aac agc Ц Н z Ŋ \Box 召 gat άς kgg rtt gac ytt യ ജ Ŋ \triangleright \Box 니 년 Д ggg gac t, Kg Z L ď А Д Ŋ \vdash ggc crt tac 田足 Ŋ ⋈ α Ŋ \mathcal{O} ggg ctg G E org aaa awc ¢ Ы Ċ 呂 HZ ctc ctc ctc 凶 니 니 凶 ď П ctg gsc cac ctg Ė Þ 口 П \triangleleft \triangleright $S_{\rm tya}$ gaa tat gaa gaa 口 \succ 闰 闰 闰 Þ gtg ttc agc ഥ Ŋ \triangleright ⋈ Пõ Н ttt ayt gga ggc Ö ᄄ $\vdash\vdash\vdash$ r Ç ø ctg agg arc 召 Ŋ abla召 ≥ Ц Н gtc tgt gct R Q Cra \mathcal{O} ď \succ \triangleright ď gyc O L ctg 디 Н \triangleleft 니 z ctc aga art att $\Omega(Z)$ r Н α Н П gtg ctg ctg arg П \triangleright 召 民民 口 口 ata aat tac ata gat ytc att ß Н Z Ц Н വ gac agg agc kgg H α **დ** Д Ŋ gat D(D) # tcc tkg IJ ⊠ Д Д Ŋ K, tgg agg H Grc tac agg വ് 卍 ⊱ ⋈ S ctc aaa r 凶 HZ Þ Ы agg ctg Q R E 口 Н 노 召 \exists ctc G B gst gaa 闰 ď 耳 П Ц tac S L Ċ × 闰 闰 闰 tac ttt Q ☐ Ş tgg r Ŋ \triangleright ≥ ĪΉ

agg

kgg

gct

gtg

gat

gct

acc

gct

aac

ata

agg

ctc

Segment 26

Segment 25

П Н ď 召 \mathcal{O} Þ വ് Õ ď > 团 \vdash > α О ⊣ \mathcal{Q} 闰 ď > ď

Н

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V A Q R A G R A I L H I P R R I R Q	T N M	aca gac aga rtc att gag gtc gyc caa agg gct kgg aga gcc att ctg mat atc cct asa aga atc aga cag	RQGLERALL	Ŀ	ctc mac att ccc asg agg att agg caa ggc γ tt gag aga gcc ct c ctg
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D R		ac ag	Н		ac at
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H			Н		
	<u>დ</u>	gra kgg	Н		t atc
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		att gcc gtc gcc ;	ტ	Z	aga gcc kgg agg gct
ď		t ga	ď		ရ ရ
H		at	民		ag

Segment 1	Segment 2	Segment 3	Segment 4	Segment 5	Segment 6
M G G K W S K S S L V G W P E V R E R I R Q T P P A A E G V C C P A A E G V atgraph aga aga aga aga atc aga crg rca acc cct gcc gct gag aga gtg aga gtg aga aga atc aga crg rca scc cct gcc gct gag aga gtg	VRERIROTPPAAEGVGAVSQDLDKHGAITS RAA gtc agg gaa agg att agg cra rcc sct ccc gct gcc gaa ggc gtc ggc gct gyc tcc crg gat ctg gat aag kac gga gcc mtc acc tcc	GAVSQDLDKHGAITSSNTPANNADCVWLKA By Sya gcc gyg agc cra gac ctc gac aaa kat ggc gct mtt aca agc tcc aat acc sct gcc aat aac sct gac tgt gyc tgg ctc rag gct	SNTPANNADCVWLKAQEEEGVGFPVRPQVP A E agc aac aca scc gct aac aat scc gat tgc gyg tgg ctg raa gcc cag gaa gag gaa gra gtg gga ttt cct gtg aga ccc caa gtg cct	Q E E E G V G F P V R P Q V P L R P M T Y K G A F D L S F F E E E E G V G F P G I S F F E Caa gag gaa gag gag gag gag gcc ccc gcc agg gcc ccc c	LRPMTYKGAFDLS $\overrightarrow{(F)}$ FLKEKGGLEGLVYSK KA LRQ GLEGLUYYSK KA VL LONG SON SYSKK CONTRACTOR SON

NEF OVERLAPPING SEGMENTS

Segment 7	Segment 8		Segment 9		Segment 10		Segment 11	
L K E K G G L E G L V Y S K K R Q E I L D L W V Y H T Q G F D D N N N $\stackrel{(Y)}{(Y)}$ ctc aag gaa aag gga ggc ctc gas gga ctg rtt tac tcc maa aag agg caa gas att ctg gat ctg tgg gtg tat mac aca cag gga twc	RQEILDLWVYHTQGFFPDWHNYTPGPGIRY D N Y Q	V aga cag gaw atc ctc gat ctc tgg gtc tac mat acc caa ggc twt ttc cct gac tgg cas aat tac aca ccc gga ccc gga ryc aga tac	F P D W H N Y T P G P G I R Y P L T F G W C F K L V P V D P Q	V ttt ccc gat tgg caw aac tat acc cct ggc cct ggc rya agg tat ccc ctc acc ttt ggc tgg tgc ttt aag ctc gtg cct gtg gat ccc	NIBEVE	cot otg aca tto gga tgg tgt tto aaa otg gto oco gto gao oct ags gaa gtg gaa gag ryo aac raa ggo gaa aac aat tgo oto otg	REVEEINKGENNCLLHPMSQHGMEDEEREV S A E	agw gag gto gag gaa ryc aat rag gga gag aat aac tgt ctg ctc cac cct ats rgt cwg cat ggc atg gaa gac gaa gas aga gag gtc

Segment 12	Segment 13
DEERREVIN WRFDSRLARRHIA Segment 12 DK BAG gag gaa gtg ctg awa tgg aaa ttc gat agc crt ctg gct ckc agg cat ats gct	LIWKFDSRLARRHIARELRPEFYKDC K K Ctc awa tgg aag ttt gac tcc crc ctc ccc ckg aga cat ats gcc aga aga aga aga aga aga aga aga aga
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g ag	RH F
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H. P. M. S. Q. H. G. M. E. J. I. C. L. cat ccc ats rgc cwa cac gga atg gag	ш tt tt tt
ນບະ	a ag
ats H 🗷	W tgg
મ કુ	H X awa
cat E	L etc

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															5
ATC/ATT			ATS/ATK	AWC/AWT	WTC/WTT	AKA/	MIC/MIT	AKC/AKT	AYC/AYT	RTC/RTT	/ KTAK	HWE/			
I Ile			Ξ	H	H	ΙR	끕	IS	II	IΛ	-	4			
CAC/CAT			MAC/MAT	SAC/SAT	CAM/CAW	CRC/CRT	CWC/CWT	CMC/CMT	YAC/YAT						
H His	Acids		HN	日	Ę,	H	出	HP	ΗX						
G Gly GGC/GGA His	TWO or More Amino Acids		KGG/	GRC/GRT	KGC/ KGT	GRG/GRA	GSC/GST	SGC/RGA	RGC/RGT	GKG/GKC	•				
G	More		GW	8	ן ק	Ä	GA	욙	GS	ĞΩ					
gaa/gag			GAS/GAM	SAG/SAA	פוופ/פווא	GKG/GKA	RAG/RAA	GWG/GWA							
EGlu	For		E i	O, E	4 6	9	Ä	EΛ							
Q Gln CAG/CAA	Codons		CRG/CRA	SAG/SAA	אביי / הייני	CWC/CWA	MAG/MAA	CMG/CMA							
o Gla	erate		QR S	3 E	į į	3 5	Ř	δĎ							
Cys IGC/IGT	ed Degen		TGS/TGK	KGC/ KGT	EVE/ CVE	1017 / TUT	WGC/WGT	TRC/TRT							
	/ Use		₩ G	ž č	3 5	5 6	S	CX							
D Asp GAC/GAT	Frequently Used Degenerate Codons For		RAC/RAT	GAS/GMI	שמט/טמט	125 / JAD	SAC/SAT	KAC/KAT	GWC/GWT						
D Asp			NG &	Z E	ב ב	3 2	Ξ	DX	À						
N Asn AAC/AAT	The Genetic Code- First and Second Most	NC	RAC/RAT	AWC/AWT	MAG/SAK	שמיי סניי	AKC/AKI	AMC/AMT	WAC/WAT						
N Asn	and	SITI	S E	Į L	MK	1	2	I I	N						
AGG/AGA	First	NGLE PO	AKT/	TUY/UUX	ממט/טמט	ליייי ליייי	ראר/ראז	ARG/ARA	AKA/	SGC/RGA	CSC/CST	ASA/ASG	CKG/CKC	MGC/MGT	
R Arg	Code-	A S]	RM	N. C.	0	מ ג	5 1	RK I	Z ;	X,	RP	RT	RL	RS	
GGC/GCT	Genetic	TWO BASES AT A SINGLE POSITION	GMC/GMT	GSC/GST	上しい/ししい	TOA/ 2011	NCC/ NCI	RCC/RCT	GXC/GXT						
A Ala	The	TWO	AD H	AG	ΔD	0	Q [AT.	AV						

The Genetic Code- First and Second Most Frequently Used Codons

Allighe letter code

R = A or G

Y = C or T

S = C or G

W = A or T

H = A or C or T

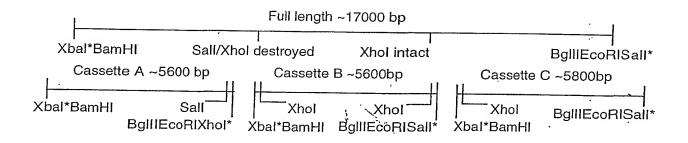
B = C or G or T

N = A or C or G

E-1

FIGURE 13

CTG/CTC			MYG/WTG TKG/TYA CWG/CWA CWC/CWT YTC/YTT MTC/MTT CYC/CYG STG/STC CKG/CKC				59	/2	1	6					
r Leu			H												
GTG/GTC			RIG/ GWC/GWT GWG/GWA KIC/KIT RIC/KIT GYC/GYT GKG/GKC STG/SIC												
v Val	cids		VM VD VE VL VG												
TAC/TAT			WAC/WAT KRC/KAT TRC/TRT TWC/TWT TWC/TWT												
$^{\rm Y}_{\rm TYT}$	More		YD YC YH YS												
TGG/	TWO or		WGG/YGG KGG/ TKG/ TKG/TGK												,
W Trp	For		MR MS ML MC												
ACC/ACA	e Codons		AYG/ AWC/AWI AWG/AWA AYG/AYA RCC/RCT ASA/ASG ASC/WCC												FIGURE 13 (cont)
T Thr	nerat		TN TX TI TA TA TS												Œ 1.
AGC/TCC	sed Dege		TSG/ ARC/ART TYG/TYA WGC/WGT TYC/TYT TYC/TYT AKC/AKT KCC/KCT KGC/RGT YCC/YCT ASC/WCC												FIGUR
Ser	:ly u		S S S S S S S S S S S S S S S S S S S												
ccc/ccr	Frequent		CMG/CMA CCC/CMT CCC/CMT CCC/CMT VCC/CMT VCC/CMT												
P Pro	Most		2 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4												
TTC/TTT	Second	TON	TKC/TKT WTC/WTT YTC/YTT TYC/TYT TWC/TWT KTC/KTT												-
r Phe	and	CIISC	FI FI FI FV FV												
ATG/	e- First	SINGLE P	AKT/ ATS/ATK MTG/WTG AWG/ AYG/ RTG/	ode										or T	
M Met	Code	67 ₹ -	MR MI MK MT MV	er cc						or T	or T	or G	or T	or G	
AAG/AAA	Genetic	BASES	ANG/ AAS/AAM MAG/WAA RAG/RAA ARG/ARA AMG/AMA AWG	le lett	A or G	C or I	G or T	Corg	A or T	Aorc	Corg	A or C	A or G	Aorc	
K Lys	The	TWO	Z Z Z Z Z Z Z Z Z Z Z Z Z Z Z Z Z Z Z	Sinc	요 	II ≯	X =	II	 <u>X</u>	# H	<u>면</u>	= ^	П Д	II Z	
	M Y V L AAG/AAA Met AIG/ Phe TIC/TIT Pro CCC/CCT Ser AGC/TCC Thr ACC/ACA Trp TGG/ Tyr TAC/TAT Val GTG/GTC Leu	M Y V U L ANG/AAA Met ATG/ Phe TTC/TTT Pro CCC/CCT Ser AGC/TCC Thr ACC/ACA Trp TGG/ Tyr TAC/TAT Val GTG/GTC Leu Genetic Code- First and Second Most Frequently Used Degenerate Codons For TWO or More Amino Acids	M AAG/AAA Met ATG/ F Phe TTC/TTT Pro CCC/CCT Ser AGC/TCC Thr ACC/ACA Trp TGG/ Tyr TAC/TAT Val GTG/GTC Leu Genetic Code- First and Second Most Frequently Used Degenerate Codons For TWO or More Amino Acids BASES AT A SINGLE POSITION	Amag/ama Mat Alicy Fig. Fig	Fe the TTC/TTT Pro CCC/CCT Ser AGC/TCC Thr ACC/ACA Trp TGG/ Tyr TAC/TAT Val GTG/GTC Leu LITEL and Second Most Frequently Used Degenerate Codons For TWO or More Amino Acids LE POSITION ATR FI WTC/WTT PH CWC/CMT SI WTC/ART TW AMC/AMT WG KGG/ YGG YM WAC/WAT VF KCC/KTT TW AMC/AMT WG KGG/ YGG YM WAC/WAT VF KCC/KTT TW AMC/AMT WG KGG/ YGG TGC/KTT TW AMC/AMT WG TGC/KTT TW AMC/AMT TGC/KTT TW AMC/AMT TGC/KTT TW AMC/AMT TGC/KTT TW AMC/AMT	Fig. 17C/TTT	ITER and Second Most Frequently Used Degenerate Codons For Two or More Amino Acids LEPOSITION Post TRC/TRT PA CRC/CRT Ser Adc/TCC Thr ACC/ACA Trp TGG/ Tyr TAC/TAT Val GTG/GTC Leu CTG/CRT Val GTG/GTC Leu CTG/CTC Leu CTG	Fe TTC/TTT Pro CCC/CCT Ser AGC/TCC Thr ACC/ACA Trp TGG/ Tyr TAC/TAT Val GTG/GTC Leu CTG/CT Lirst and Second Most Frequently Used Degenerate Codons For TWO or More Amino Acids LE POSITION Total Column	Fe	LITEL and Second Most Frequently Used Degenerate Codons For Two or More Amino Acids LEP POSITION ATT TWO/TWT PA COC/CCT Ser AdC/FCC This ACC/ACT TWO OR TYP TWO/TWT PA COC/CCT Ser AdC/ACT TW ANG/ANT WE TSG/ TYP TWO/TWT PA COC/CCT SER TWO/TWT TR ASS/ASS TWO/TWT TR ASS/ASS TWO/TWT TR ASS/ASS SER TWO/TW TR ASS/ASS SER TWO/TW TR ASS/ASS SER TWO/TW TR ASS/ASS SER TWO/TW TR ASS/ASS SER TWO/TW TR ASS/ASS SER TWO/TWO TR A	Fe	Fe	F	Fig. 1707/177 Fig. 1707/17	Second S



Full length construction after cloning the cassettes into pBS-Sites marked with a "*" are in the pBS MCS

Cassette Extras (Can be removed from cassette ends)

A (37bp)		BamHI/Kozak Start	Sall Stop	Bglll	EcoRi	
D (40hn)	5'	gc ggatccacc atg	gtcgac tga	agatct	gaattc	gc 3'
		BamHI/Kozak Start Xhol	Xhol Stop	Bglll	EcoRi	
0 (071)	5'	gc ggatccacc atg ctcgag				gc 3'
		BamHI/Kozak Start Xhol	Stop	Bglll	EcoRI	_
	2,	gc ggatccacc atg ctcgag	tga	agatct	gaattc	gc 3'

FIGURE 14

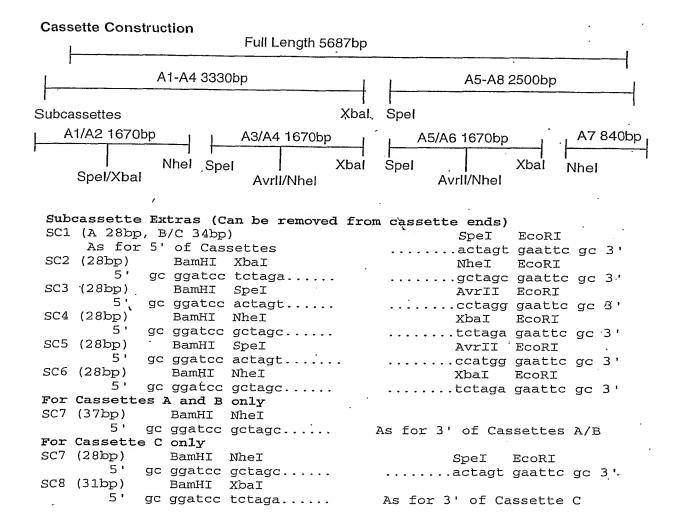


FIGURE 14 (Cont)

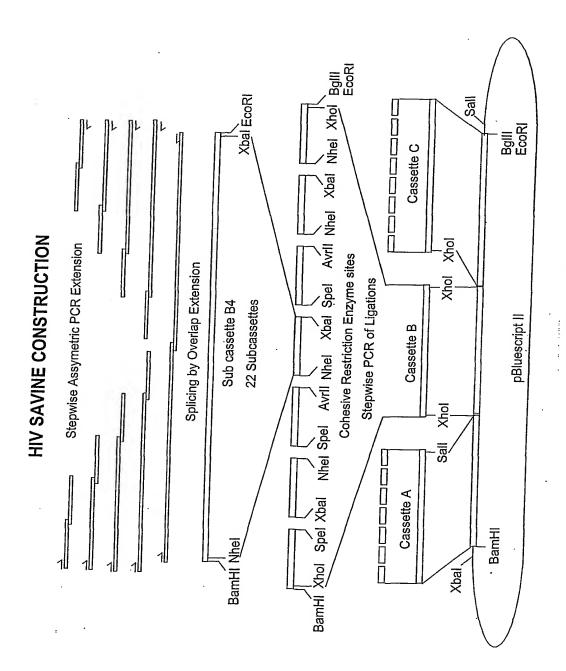
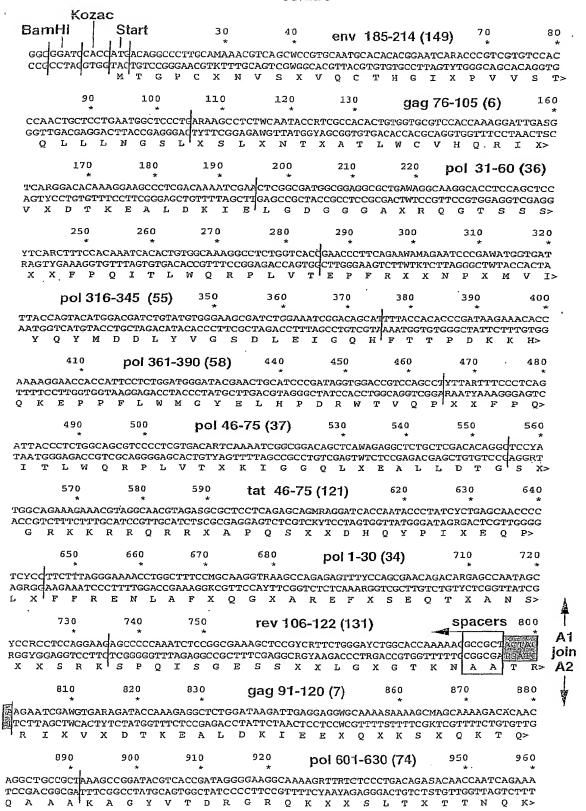
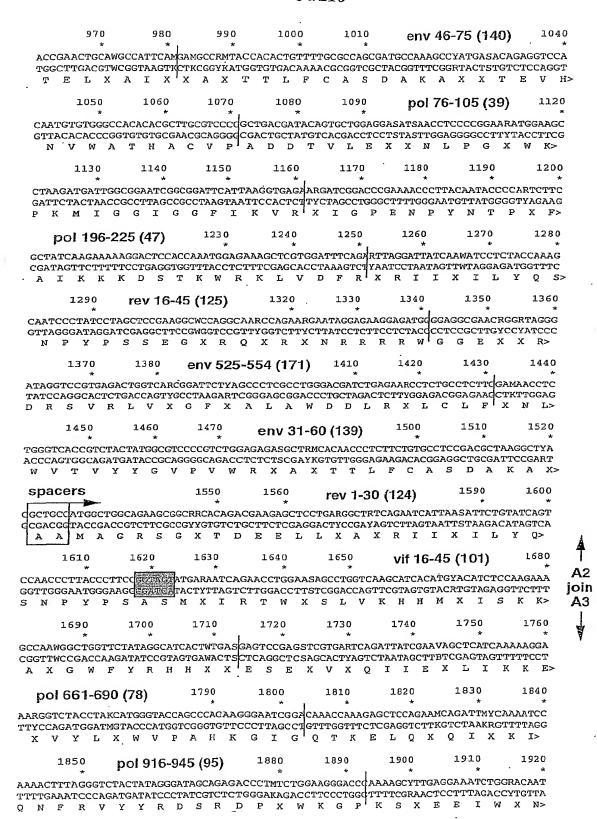


FIGURE 14 (Cont)

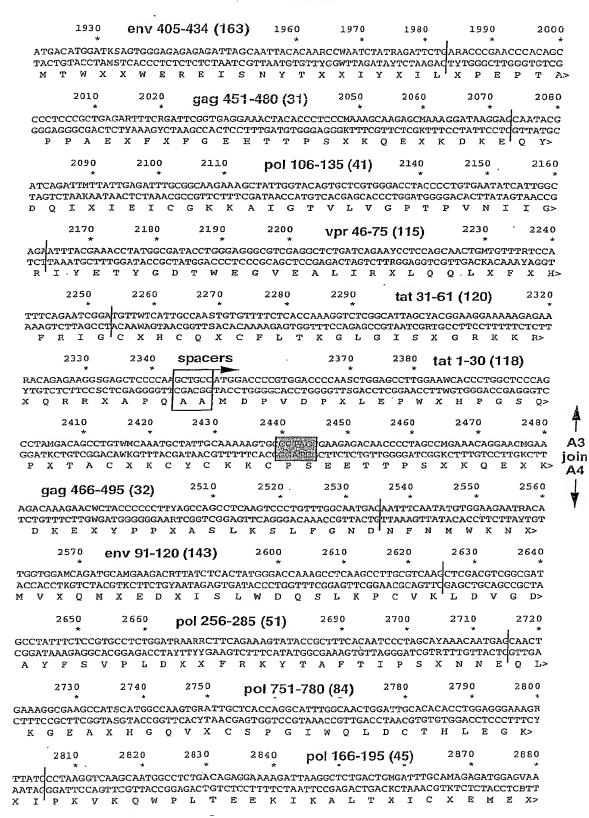
63/216



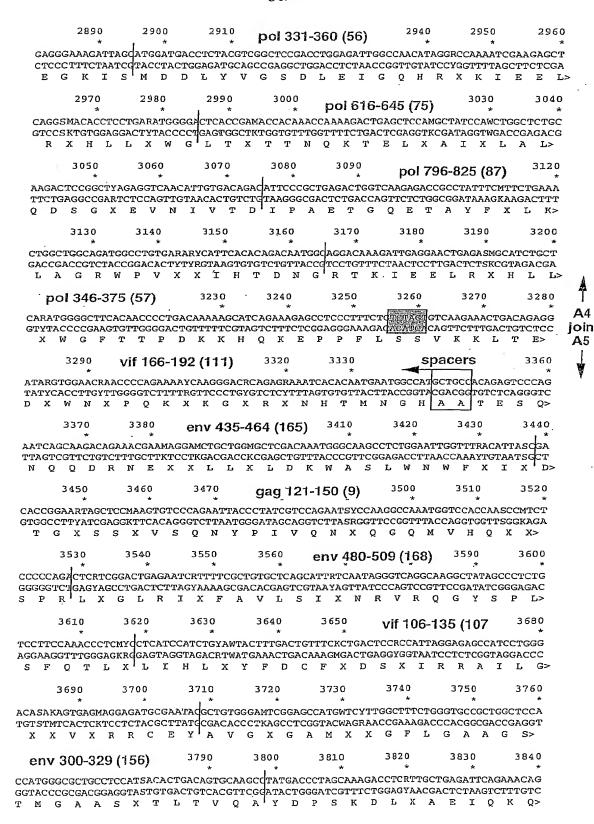
64/216



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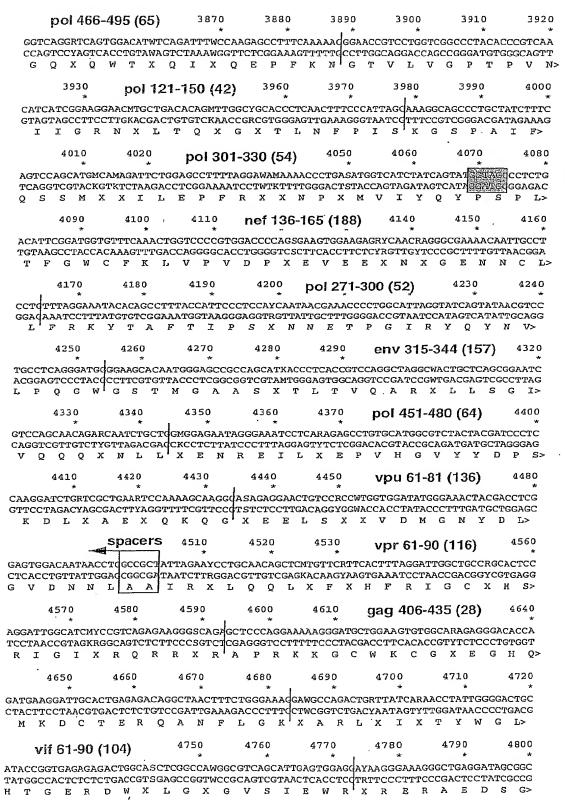


FIGURE 15 (Cont)
SUBSTITUTE SHEET (RULE 26)

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vpu 46-75 (135) 4830 4840 4850 4860 4870 4880 AACGAAAGCGAAGGCGACASAGAAGAGCTCAGCRCAWTGGTGGACATGGGCCAATTACGATCTGTTAGGCCCCCCAG TTGCTTTCGCTTCCGCTGTSTCTTCTCGAGTCGYGTWACCACCTGTACCCGTTAATGCTAGACAGAGAGAGGGGGGTC NESEGDXEELSXXVDMGNYDLS 4890 4930 4950 4920 4940 4960 env 510-539 (170) GGGACCCGATAGGCYGGRGRGAATCGAAGAGGAAGGCGGAGAGCRAGRCAGAGRCAGAAGCGTCAGGCTCGTGARTGG(A CCCTGGGCTATCCGRCCYCYCTTAGCTTCTCCTTCCGCCTCTCGYTCYGTCTCYGTCTTCGCAGTCCGAGCACTYACCG P D R X X X I E E E G G E X X R X R S V R L V X 4980 5010 nef 151-180 (189) GMGAGGTCGAGGAARYCAATRAGGGAGAGAATAACTGTCTGCTCCACCCTATSRGTCWACATGGCATGGAAGAGACGAAGA CWCTCCAGCTCCTTYRGTTAYTCCCTCTTATTGACAGACGAGGTGGGATASYCAGWTGTACCGTACCTTCTGCTTCTS X E V E E X N X G E N N C L L H P X X X H G M E D E X> 5050 5060 5070 5110 5100 5120 pol 961-990 (98) agagaggt aatagcgatatcaaagtggtccccagaaggaaagccaaaatcattagggattacggaaagcaaatggctgg TCTCTCCAGTTATCGCTATAGTTTCACCAGGGGTCTTCCTTTCGGTTTTAGTAATCCCTAATGCCTTTCGTTTACCGACC
R E V N S D I K V V P R R K A K I I R D Y G K Q M A G> 5150 5190 5130 5140 5160 pol 16-45 (35) 5200 CGMTGACTGTGTGGCCRGdTTCYCTTCCGAGCAAACARGGGCTAACTCCYCTRCAAGCAGAAAGCTGGGAGACGGAGGCG GCKACTGACACCGGYCGAAGRGAAGGCTCGTTTGTYCCCGATTGAGGRGAYGTTCGTCTTTCGACCCTCTGCCTCCGC X D C V A X F X S E Q T X A N S X X S R K L G D G G> 5210 5220 5230 5240 5250 gag 390-420 (27) GAGCCGASAGACAGGGAACAAGCTCCAG5300 5310 5330 5340 5350 5290 5320 5360 CGCAAGAAAGGTTGTTGGAAATGCGGAARGGAAGGCCA¶CAAATGAAAGACTGTACCGAAAGGCAAGCCAATTTCCTCGG GCGTTCTTTCCAACAACCTTTACGCCTTYCCTTCCGGTAGTTTACTTTCTGACATGGCTTTCCGTTCGGTTAAAGGAGCC RKKGCWKCGXEGH^IQMKDCTERQANFLG> gag 421-450 (29) 5390 5400 5410 5420 5430 5440 CAAAATCTGGCCCTCCMRCAAAGGCAGACCCGGAAACTTTCYCCAAAGdAAMTGGCTCTGGTATATCAAAATCTTTATCA GTTTTAGACCGGGAGGKYGTTTCCGTCTGGGCCTTTGAAAGRGGTTTC(TTKACCGAGACCATATAGTTTTTAGAAATAGT KIWPSXKGRPGNFXQSXWLWYIKIFI> 5450 5480 5490 5500 5510 env 465-494 (167) TGATCGTCGGTGGACTGRTTGGCCTCAGGATTRTCTTTGCCGTCCTGTCCATCRTTAAQGGAGCCGYGAGCCRAGACCTC ACTAGCAGCCACCTGACYAACCGGAGTCCTAAYAGAAACGGCAGGACAGGTAGYAATTGCCTCGGCRCTCGGYTCTGGAG V G G L X G L R I X F A V L S I X N G A X S X D L> 5530 nef 31-60 (181) 5570 5580 spacers GATAAACATGGCGCTMTTACAAGCTCCAATACCSCTGCCAATAACSCTGACTGTGYCTGGCTGRAGGC¶GCTGCQATGAC CTATTTGTACCGCGAKAATGTTCGAGGTTATGGSGACGGTTATTGSGACTGACACRGACCGACYTCCGACGGTACTG D K H G A X T S S N T X A N N X D C X W L X A A A M T> 5620 5630 5660 5610 vpu 1-30 (132) ACCCCTGGAGATCATCGCTATCGTCGCCYTTATCGTCGCCCTCATCMTAGCCATTGTGGTCTGGACAATCGYCTWCATTG TGGGGACCTCTAGTAGCGATAGCAGCGGRAATAGCAGCGGGAGTAGKATCGGTAACACCAGACCTGTTAGCRGAWGTAAC PLEIIAIVAXIVALIXAIVVWTIXXI> 5700 5710 5720 5690 pol 136-165 (43) AGTA GREEN AATMTGCTCACCCAAMTCGGAYGCACACTGAATTTCCCTATCTCCCCCATTGASACAGTGCCTGTGAAA TCAT / CASC GTTAKACGAGTGGGTTKAGCCTRCGTGTGACTTAAAGGGATAGAGGGGGTAACTSTGTCACGGACACTTTN X L T Q X G X T L N F P I S P I X T V P V K>

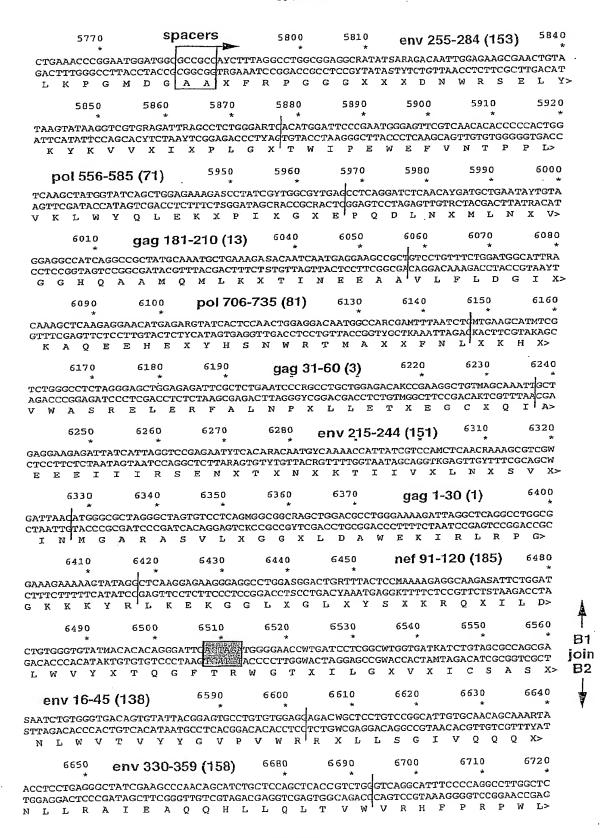
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A6

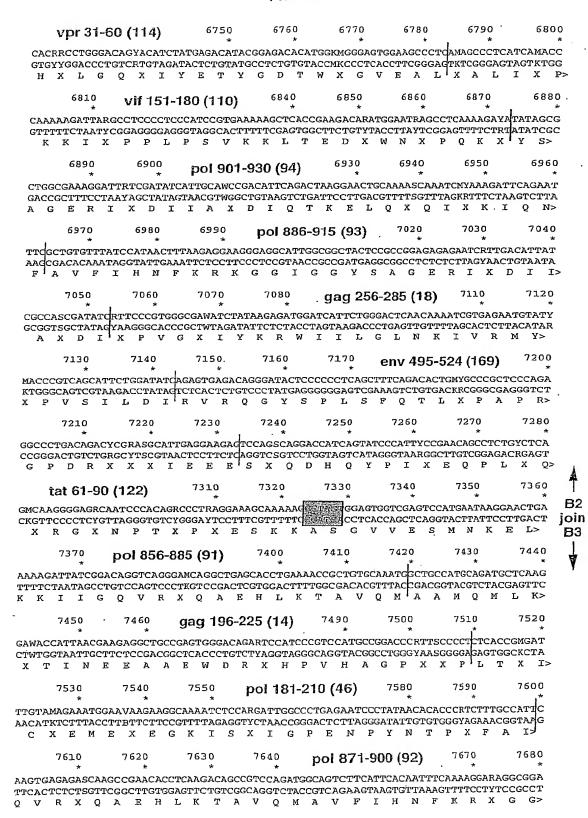
join

A7

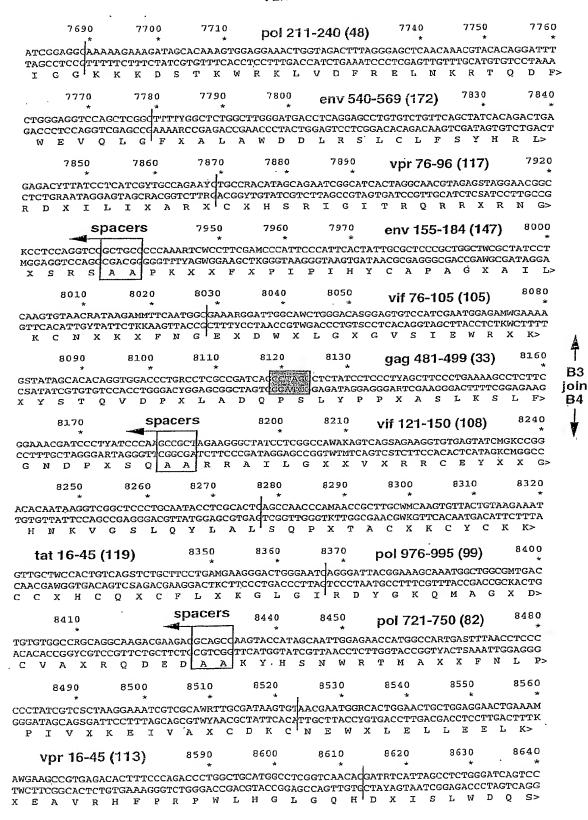
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71/216



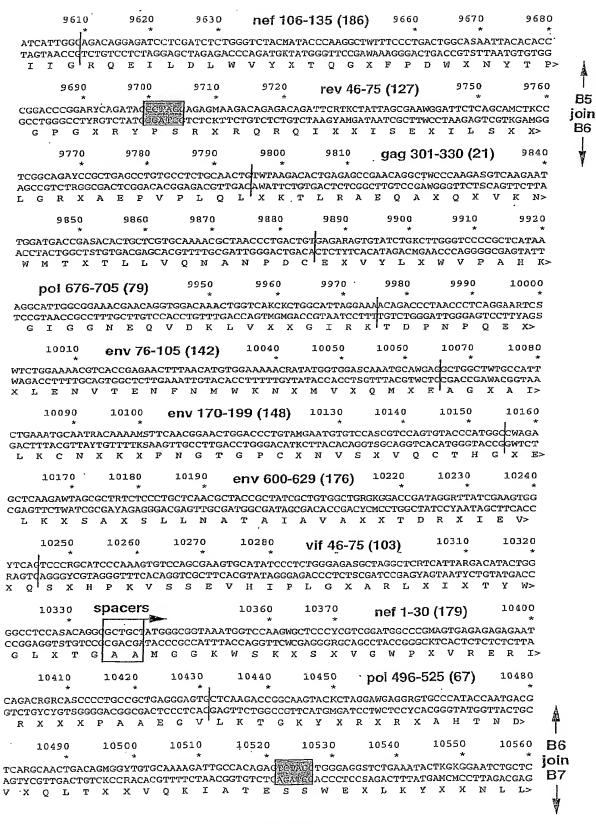
72/216

8650 env 106-144 (144) 8680 8690 8700 8710 8720 $\tt CTGAAACCCTGTGTGAAACTGACACCCCTCTGCGTCACCCTCAACTGTACCAATGCCAATCTqMwgaagagmtactccac$ L K P C V K L T P L C V T L N C T N · A N L | X K X Y S T> 8730 8740 8770 8780 8800 8790 vif 91-120 (106) CCAAGTGGACCCCGRTCTGGCTGACCAWCTGATTCACCTCCACTATTTCGATTGCTTTKCCGATAGCRCAATCCATCCCA $\tt GGTTCACCTGGGGCYAGACCGACTGGTWGACTAAGTGGAGGTGATAAAGCTAACGAAAMGGCTATCGYGTTACGTAGGGT$ Q V D P X L A D X L I H L H Y F D C F X D S X I H P> 8810 8820 8830 nef 166-195 (190) 8860 TSRGCCWACACGGAATGGAGGATGAGGAWAGGGAAGTGCTGAWATGGAAATTCGATAGCCRTCTGGCTCKCAGGCATATS ${\tt ASYCGGWTGTGCCTTACCTCCTWTCCCTTCACGACTWTACCTTTAAGCTATCGGYAGACCGAGMGTCCGTATAS}$ X X X H G M E D E X R E V L X W K F D S X L A X R H X> 8890 8900 8910 8920 poi 151-180 (44) 8950 GCTTTTCGAWACCGTCCCCGTCAAGCTCAAGCTCGCATGGACCCAAAGTGAAACAGTGGCCCCTCAC CGALLEGGATAGCTWTGGCAGGGCAGTTCGAGTTCGGACCGTACCTGCGTTTCACTTTGTCACCGGGGAGTG PIXTVPVKLKPGMDGPKVKQWPL 8970 8980 8990 9000 9010 gag 436-465 (30) 9040 CGAAGAGAAATCAAAGCQATTTGGCCTAGCMRCAAGGGAAGGCCTGGCAATTTCCYGCAGTCCARGCCTGAGCCTACCG GCTTCTCTTTTAGTTTCGGTAAACCGGATCGKYGTTCCCTTCCGGACCGTTAAAGGRCGTCAGGTYCGGACTCGGATGGC E E K I K A I W P S X K G R P G N F X Q S X P E P T> 9050 9060 9070 9080 9090 vif 31-60 (102) CACCCCCAGCCGAGARCTTTRGATTCGGCATTAGCAAAAAGGCTAASGGATGGTTTTACAGACACCATTWCGAWAGCCRA GTGGGGGTCGCTCTYGAAAYCTAAGCCGTAATCGTTTTTCCGATTSCCTACCAAAATGTCTGTGGTAAWGCTWTCGGYTA PPAEXFX FX FG ISKKAXG WFYRHHXXSX> 9130 9140 9150 9160 9170 9180 9190 9200 CACCCTAAGGTCAGCTCCGAGGTCCACATTCCCCTCGGGATGATGACCGCTTGCCAAGGCGTCGGCGGACCCRGTCACAA GTGGGATTCCAGTCGAGGCTCCAGGTGTAAGGGGAGCCCTACTACTGGCGAACGGTTCCGCAGCCGCCTGGGYCAGTGTT H P K V S S E V H I P L G M M T A C Q G V G G P X H K> gag 346-375 (24) 9230 9240 9250 9260 9270 AGCCAGGGTACTGGCAGAGGCTATGTCCCAGGYGAMCMACGCTAACATTCCTCCCATTGTGSCCAAAGAGATTGTGGCAW TCGGTCCCATGACCGTCTCCGATACAGGGTCCRCTKGKTGCGATTGTAAGGGGGGTAACACSGGTTTCTCTAACACCGTW
A R V L A E A M S Q X X X A N I P P I V X K E I V A> 9290 pol 736-765 (83) 9320 9330 9340 9350 9360 $\tt RCTGTGACAAATGCCAGCTCAAGGGTGAGGCTATKCACGGACAGGTGRACTGTAGCCCTTCCGAGGGAWCAAGACAGRCT$ YGACACTGTTTACGGTCGAGTTCCCACTCCGATAMGTGCCTGTCCACYTGACATCGGGAGGGCTCCCTWGTTCTGTCYGA X C D K C Q L K G E A X H G Q V X C S P S E G X R Q X> 9380 rev 31-60 (126) 9410 9420 9440 AGGARGAACAGACGTAGAAGGTGGCGTGMGAGGCAAAGGCAAATCCRCKCCATCTCCGAGWGGATTCTGGGACAGATRAG TCCTYCTTGTCTGCATCTTCCACCGCACKCTCCGTTTCCGTTTAGGYGMGGTAGAGGCTCWCCTAAGACCTGTCTAYTC R X N R R R R W R X R Q R Q I X X I S E X I L G Q X R> 9450 9460 9470 9500 9510 gag 226-255 (16) GGAACCCAGAGGCTCCGACATTGCCGGTACCACAAGCACTGCAAGAGCAAATCGSATGGATGACAARCAATCCCCCTR EPRGSDIAGTTSTLQEQIXWMTXNPPJ 9550 pol 841-870 (90) ${\tt RCATTMAGCAAGAGTTTGGCATTCCCTATAACCCTCAGTCCCAGGGCGTCGTGGAAAGCATGAACAAAGAGCTCAAGAAA}$ $\tt YGTAAKTCGTTCTCAAACCGTAAGGGATATTGGGAGTCAGGGTCCCGCAGCACCTTTCGTACTTGTTTCTCGAGTTCTTT$ X I X Q E F G I P Y N P Q S Q G V V E S M N K E L K K>

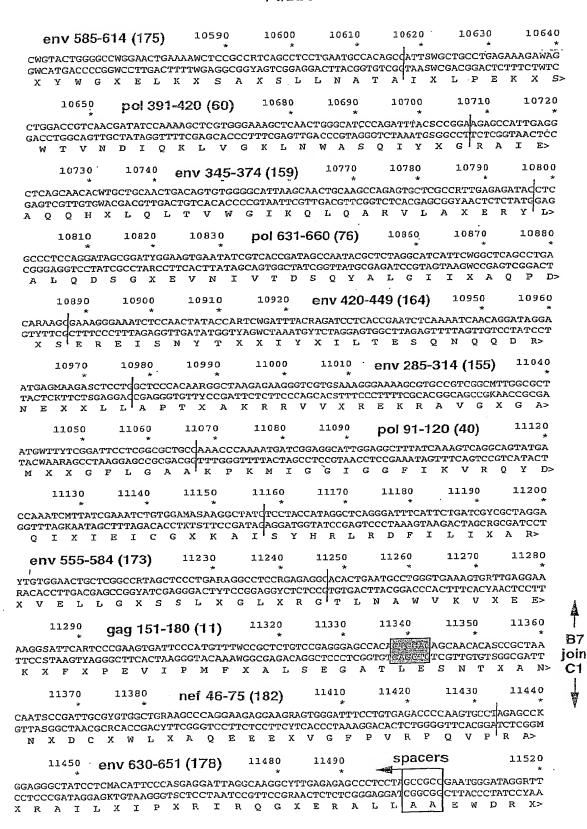
FIGURE 15 (Cont)
SUBSTITUTE SHEET (RULE 26)

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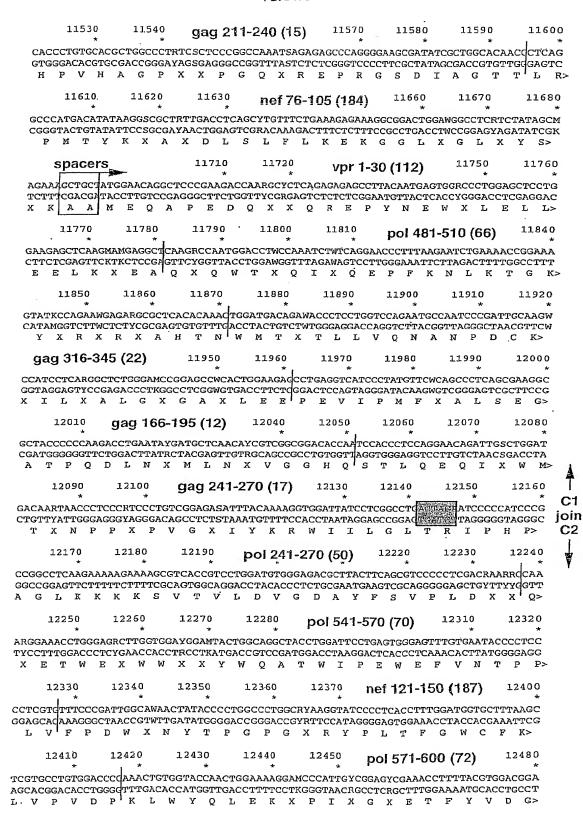
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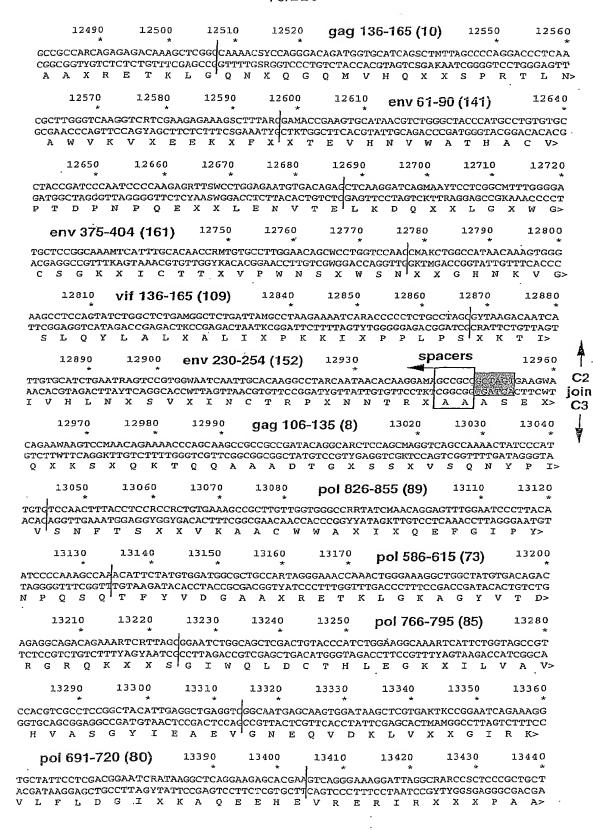
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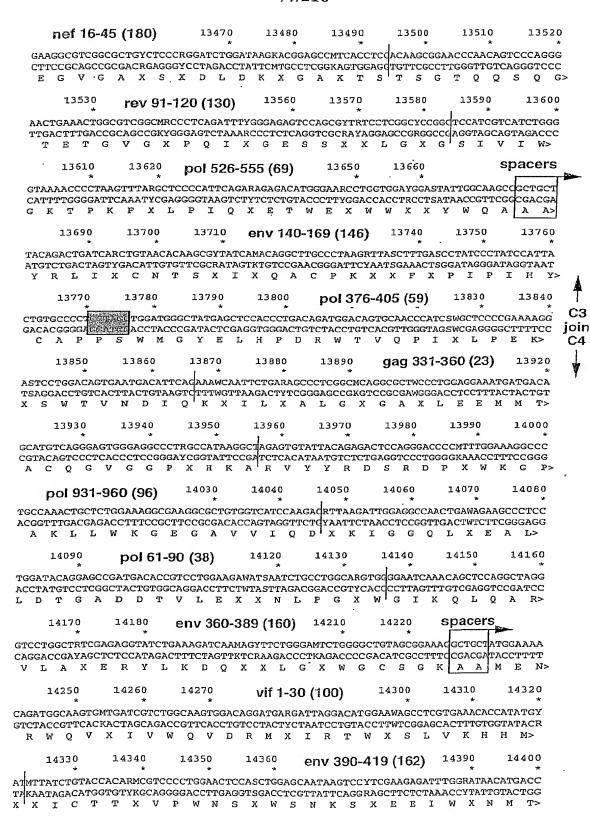
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78/216

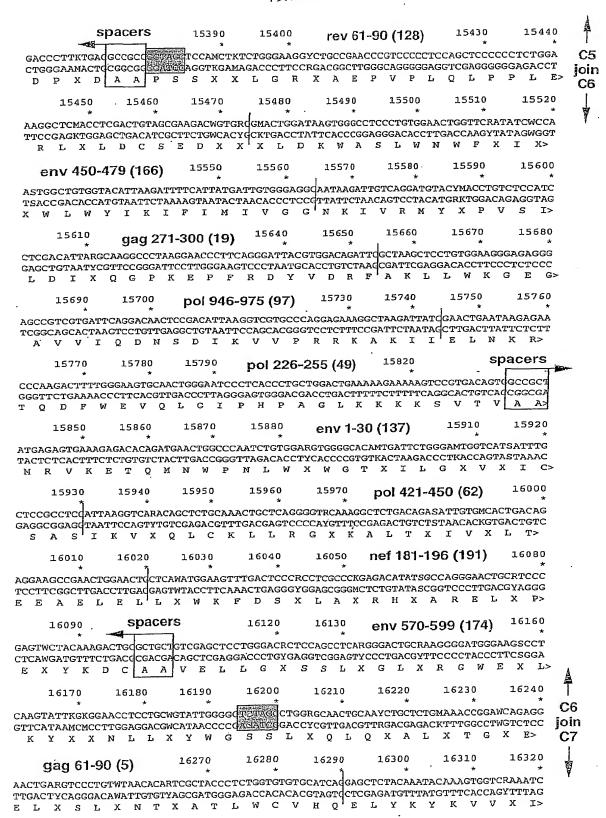
C4

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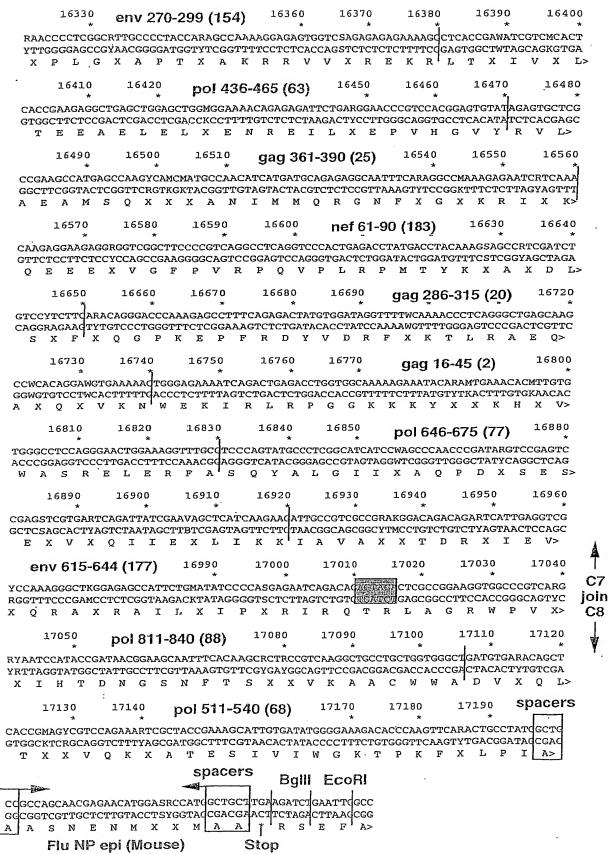
C5

14410 14420 14430 vpu 16-45 (133) 14460 14470 14480 ${\tt TGGATKSAATG}$ $\mathtt{ACCTAMSTTAC} d$ GACTAAKAGCGATAGCAGCACCACCTGGTAACRCAWATAGCTTATGTYCTTTGACGAGTYCGTTTCCTY W X X W L I X A I V V W T I X X I E Y X K L L X Q R X> 14490 14500 14510 14520 gag 46-75 (4) 14550 AATCGATAGGCTCATCRAAAGGCTCAACCCTGGCCTCCTGGAAACCKCTGAGGGATGTMAACAGATCCTGGRACAGCTCC TTAGCTATCCGAGTAGYTTTCCGAGTTGGGACCGGAGGACCTTTGGMGACTCCCTACAKTTGTCTAGGACCYTGTCGAGG 14580 14590 14600 14610 14640 AGYCCGCCCTCMAGACAGGCWCCGAAGAGCTCTTTTTAG TCRGGCGGGAGKTCTGTCCGWGGCTTCTCGAGAGAGTTTCTTTCGAGGACTYTGTCTCTTYCTAACTGTCTGACTAAYTC QXALXTGXEEL S S R K L L X Q R X I D R L vpu 31-60 (134) 14670 14680 14690 14700 14710 AGAAYCAGAGAGAGGCCGAAGACTCCGGCAATGAGTCCGAGGGAGAACACCCGGAATCAGATACCAATACAATGTGCT TCTTRGTCTCTCTCGGCTTCTGAGGCCGTTACTCAGGCTCCCTCTGTGGGCCCTTAGTCTATGGTTATGTTACACGA R X R E R A E D S G N E S E G D T P G I R Y Q Y N V L> 14730 14760 pol 286-315 (53) 14770 . 14780 14790 CCCCCAAGGCTGGAAGGGCTCCCCASCCATTTTCCAAAGCTCCATGMCCMAAATCCTCATGATGCAAAGGGGAAACTTTA GGGGGTTCCGACCTTCCCGAGGGGTSGGTAAAAGGTTTCGAGGTACKGGKTTTAGGAGTACTACGTTTCCCCTTTGAAAT
PQGWKGSPXIFFQSSMXXILLMMMQRGNFS 14810 14820 gag 376-405 (26) 14850 14860 $\tt RGGGACMGAAAAGGATTRTCAAGTGCTTCAACTGTGGAAAGGAAGGCCATMTCGCTARGAATTGCAGGCCTCCCCTGGAG$ $\tt YCCCTGKCTTTTCCTAAYAGTTCACGAAGTTGACACCTTTCCTTCCGGTAKAGCGATYCTTAACGTCTGGAGGGGACCTC$ X G X K R I X K C F N C G K E G H X A X N C R | P P 14890 14900 14910 14940 14950 14960 rev 76-105 (129) AGACTGMACCTGGATTGCTCCGAGGATWGCGRCACCTCCGGCACAGCAAAGCCAAGGCACAGAGACAGGAGTGGGACT ${\tt TCTGACKTGGACCTAACGAGGCTCCTAWCGCYGTGGAGGCCGTGTGTCGTTTCGGTTCCGTGTCTCTCACCCT|_{GA}}$ R L X L D C S E D X X T S G T Q Q S Q G T E T G V G L> 14980 14990 15000 15030 pol 781-810 (86) ${\tt CGTGGCTGTGCATGTGGCCAGCGGATATATCGAAGCCGAAGTGATCCCTGCCGAAACTGGACAGGAAACCGCTTACTTTM}$ GCACCGACACGTACACCGGTCGCCTATATAGCTTCGGCTTCACTAGGGACGGCTTTGACCTGTCCTTTGGCGAATGAAAK V A V H V A S G Y I E A E V I P A E T G Q E T A Y F> 15050 15060 15070 15080 15090 env 200-229 (150) TCCTCAAGATTARGCCTGTGGTCAGCACACAGCTCCTGCTCAACGGTAGCCTCGCTGAAGAGGAARTCRTTATCAGAAGC AGGAGTTCTAATYCGGACACCAGTCGTGTGTCGAGGACGAGTTGCCATCGGAGCGACTTCTCCTTYAGYAATAGTCTTCG X L K I X P V V S T Q L L L N G S L A E E E X X I R S> 15130 15140 15150 15160 15170 pol 406-435 (61) ${\tt GAAAACYTTACCRATAA}$ ${\tt AAACTGGTCGGCAAACTGAATTGGGCTTCCCAAATCTACSCTGGCATCAAAGTGARGCAACT}$ CTTTTGRAATGGYTATTGTTTGACCAGCCGTTTGACTTAACCCGAAGGGTTTAGATGSGACCGTAGTTTCACTYCGTTGA
ENXTXNKLVGKLNWASQLY 15210 15220 15240 15230 15250 env 121-139 (145) ${\tt GTGTAAGCTCCTGAGAGGCRCCAAAGC} {\tt GTGTCACCCCTCTGTGTGACACTGAATTGCACAAACGCTAACCTCATCAATG}$ CACATTCGAGGACTCTCCGYGGTTTCGGGAGTGGGGAGACACACACTGTGACTTAACGTGTTTGCGATTGGAGTAGTTAC
C K L L R G X K A L T P L C V T L N C T N A N L I N> spacers 15310 15320 15360 tat 76-102 (123) TGAA†GCTGC†CAAMCCAGAGGCGATAACCCTACCGRTCCCRAAGAGTCCAAGAAARAGGTCGMGTCCAAGRCAGAGACA ACTTACGACGAGTTKGGTCTCCGCTATTGGGATGGCYAGGGYTTCTCAGGTTCTTTYTCCAGCKCAGGTTCYGTCTCTGT _A|Q X R G D N P T X P X E S K K X V X S K X E T>

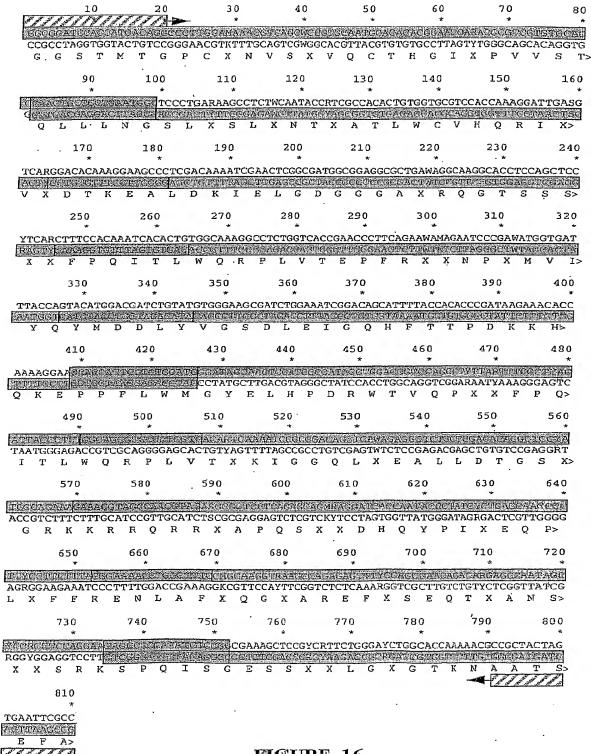
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EIGURE 16

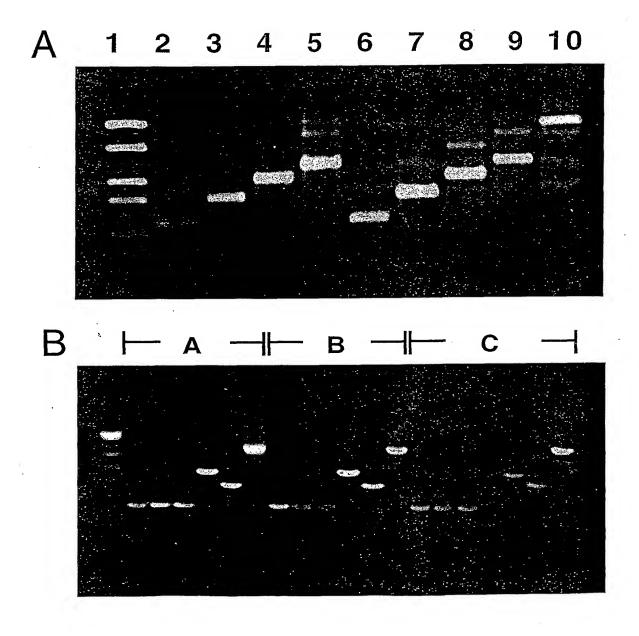


FIGURE 17

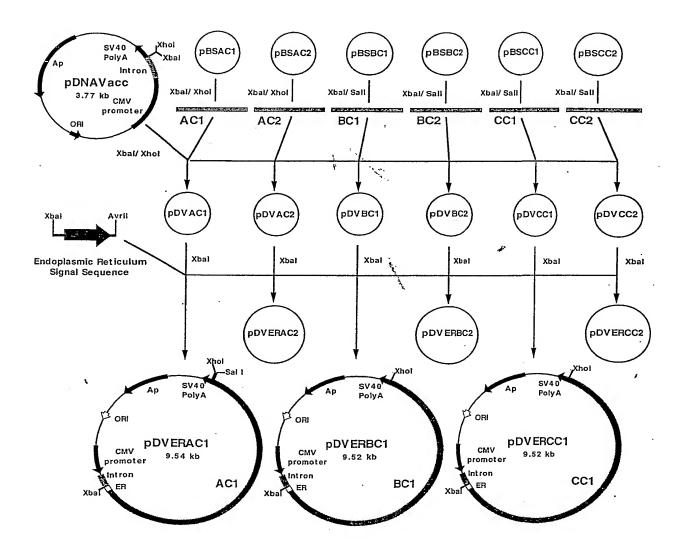
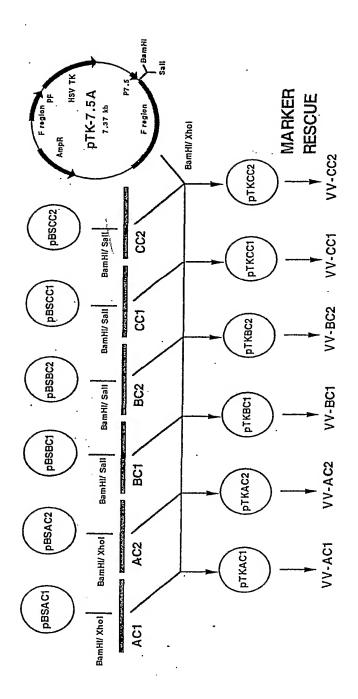


FIGURE 18A



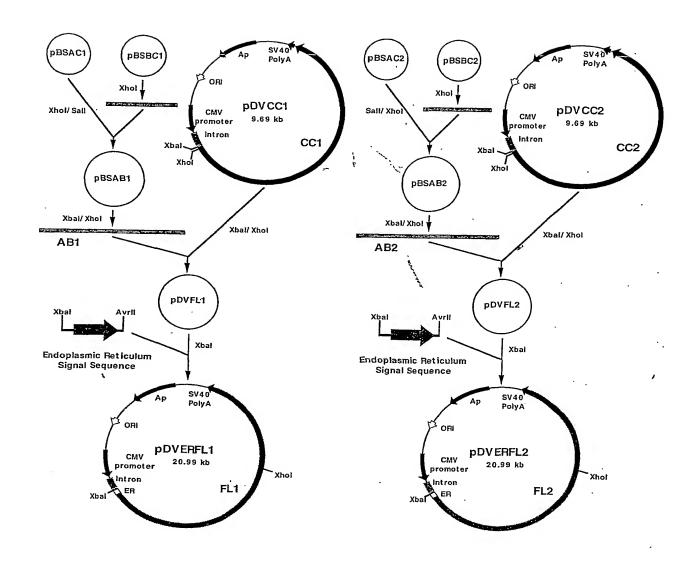
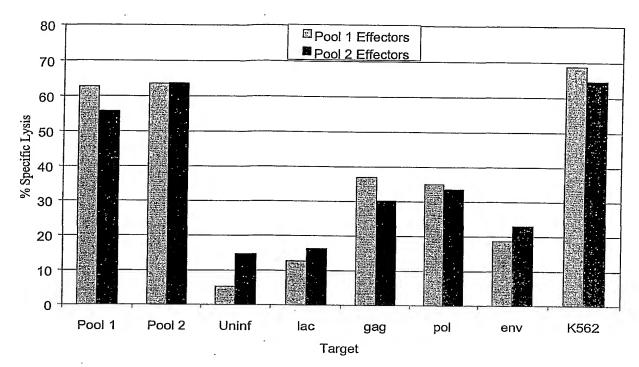


FIGURE 18C

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Subject1





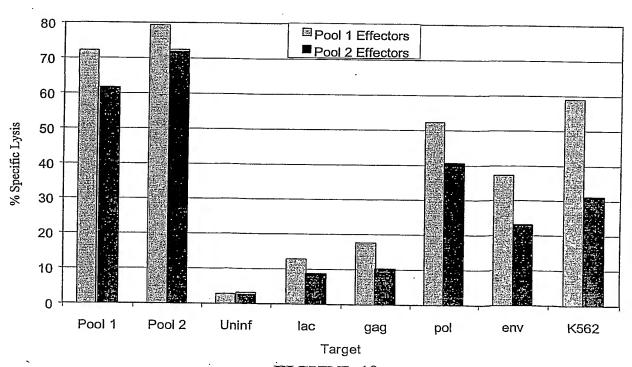
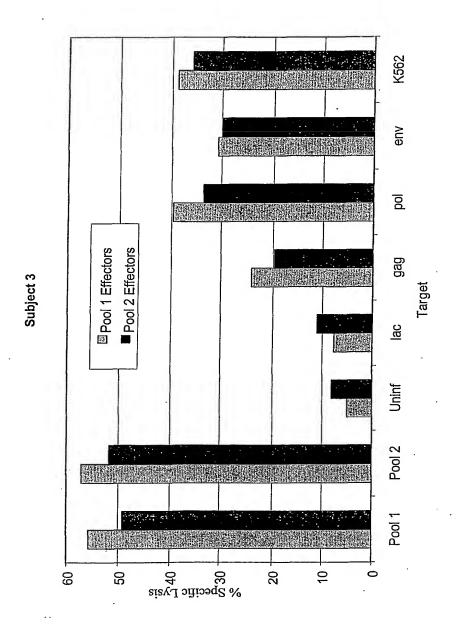


FIGURE 19

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SUBSTITUTE SHEET (RULE 26)

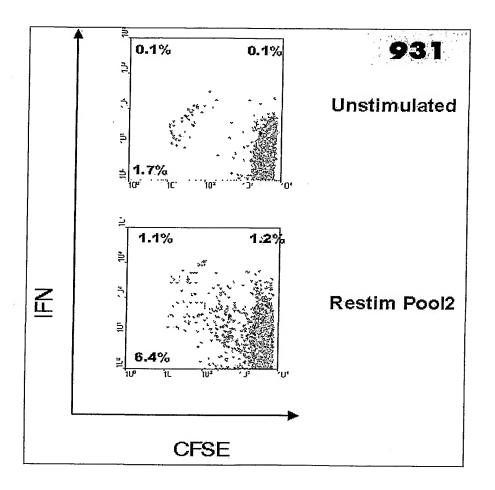


Figure 20

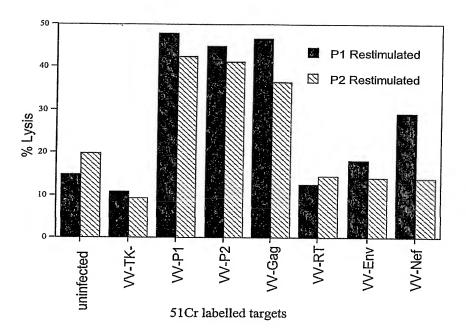


Figure 21

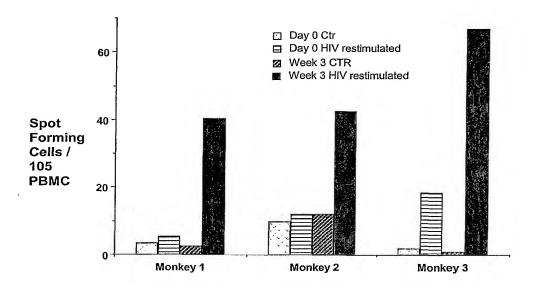


Figure 22A

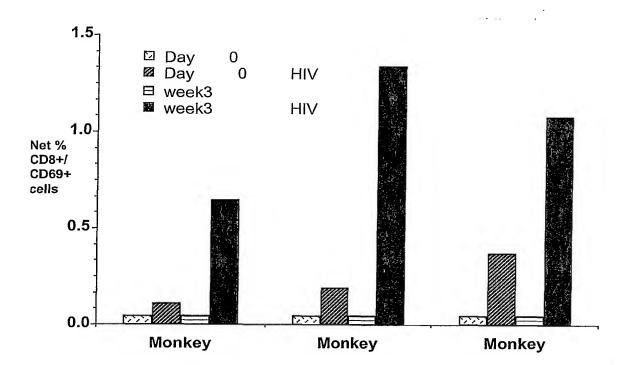


Figure 22B

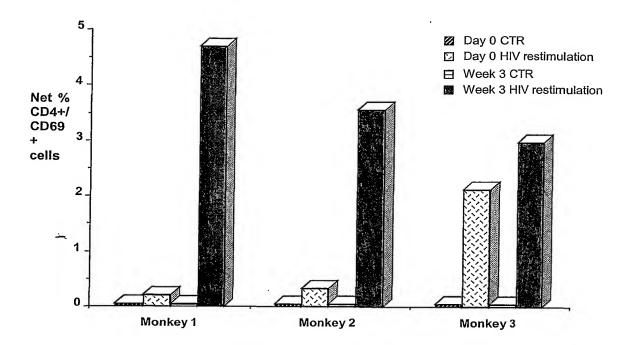


Figure 22C

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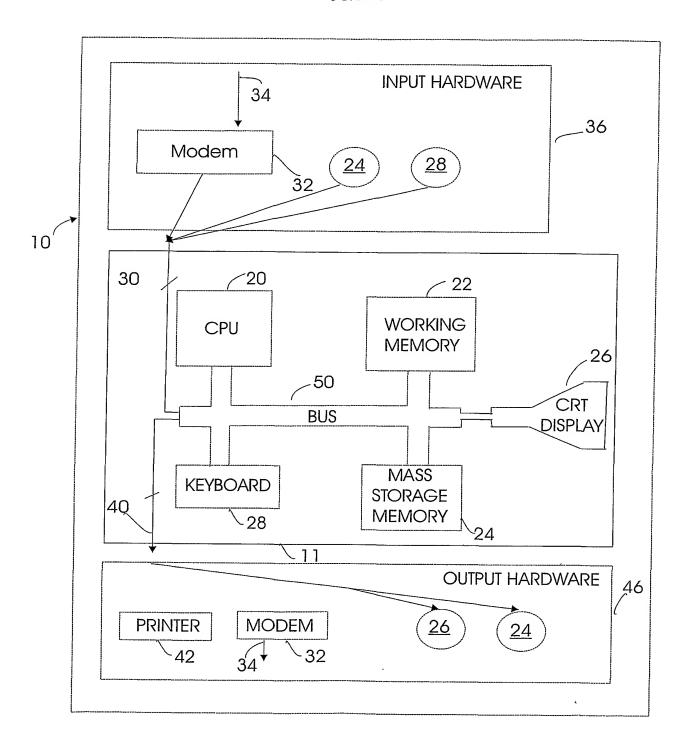


FIGURE 23

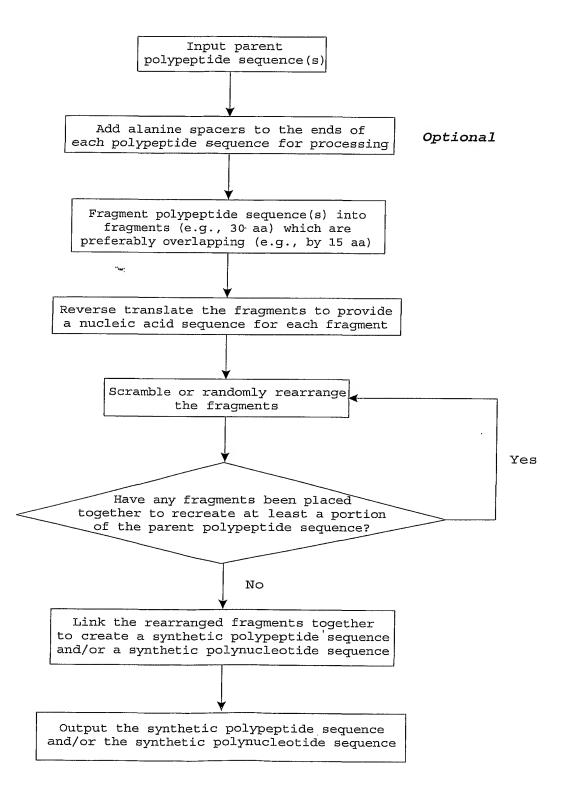


Figure 24

```
/* Scramble */
                                                 95/216
 /* Includes */
 #include <stdio.h>
 #include <stdlib.h>
 #include <string.h>
 #include <time.h>
 /* Constant definitions */
 /* Version Information */
 #define VERSION_NO
                                                                  "0.2"
 #define VERSION_DATE
                                                       "04/03/1999"
 /* Misc */
 #define KEYBOARD BUFFER SIZE
                                            256
                                                                  /*size of keyboard read buffer */
 #define LEN CODON
                                                       4
                                                                            /*length of codon (including
 #define BUFFER SIZE
                                                                  10000
                                                                            /*size of file read buffer */
 #define TRUE
                                                                  1
                                                                                       /*boolean true */
 #define FALSE
                                                                  0
                                                                                       /*boolean false */
 /* Error codes */
#define E_NOERROR
                                                       0
                                                                            /*no error */
#define E_NOINFILE
                                                       1
                                                                            /*genes file not found */
#define E_MALLOC
                                                       2
                                                                            /*memory allocation error */
#define E_FILEREAD
                                                                            /*file read error */
#define E_CREATE_OUTPUT_FILE #define E_OVERLAP
                                            4
                                                                 /*error creating output file */
                                                       5
                                                                            /*segment overlap >= length
/* Structure definitions */
typedef struct gene GENE;
typedef GENE * P_GENE;
typedef struct gene_segment GENE_SEGMENT;
typedef GENE_SEGMENT * P_GENE_SEGMENT;
struct gene {
           char * name;
           char * data;
           P_GENE next_gene;
};
int number:
          int offset;
          int first codon choice;
          char * amino data;
          char * dna data;
          P_GENE_SEGMENT next_seg;
};
```

```
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  /* Function prototypes */
  int prolog();
  int get_parameters();
  int read_int(char * prompt);
  int load_genes();
  int add_gene(char * gene_name,char * gene_data);
void insert_gene(P_GENE * head,P_GENE new_gene);
  int add_aa();
int split_genes();
 int split_gene(P_GENE g);
int insert_segment(P_GENE_SEGMENT * head_seg,P_GENE_SEGMENT new_seg);
int convert_segments_aa_to_dna();
  int convert_aa_to_dna(char * aa_ptr,char * dna_ptr,int first choice);
  char * codon(char acid_char,int preferred);
  int perform_scramble();
  int scramble_segments();
  int adjacent_segments();
  int display_genes();
  int write output file();
  void strip_newline(char * strip_str);
  void pad amino string(char * amino ptr, char * padded ptr);
 int even(int test_num);
 void read_str(char * prompt,char * string);
  char * read_nonblank_line(char * buf,int buf_size,FILE * in_file);
 int user confirmation();
 void test();
 /* Global variables */
 char * codon table[26][2] = {
char * codon_table[26][2] =
/* A 00 */ {"GCC","GCT"},
/* - 01 */ {"???","???"},
/* C 02 */ {"TGC","TGT"},
/* D 03 */ {"GAC","GAT"},
/* E 04 */ {"GAG","GAA"},
/* F 05 */ {"TTC","TTT"},
/* G 06 */ {"GGC","GGA"},
/* H 07 */ {"CAC","CAT"},
/* I 08 */ {"ATC","ATT"},
/* - 09 */ {"???","???"},
/* K 10 */ {"AAG","AAA"},
/* L 11 */ {"CTG","CTC"},
/* M 12 */ {"ATG","ATG"},
/* M 12 */ {"ATG","ATG"},
/* N 13 */ {"AAC","AAT"},
/* - 14 */ {"???","???"},
/* P 15 */ {"CCC","CCT"}
/* Q 16 */ {"CAG","CAA"},
/* R 17 */ {"AGG","AGA"},
/* S 18 */ {"AGC","TCC"},
/* T 19 */ {"ACC", "ACA"},
/* - 20 */ {"???","???"},
/* V 21 */ {"GTG","GTC"
/* W 22 */ {"TGG","TGG"},
```

Figure 25 (Cont)

```
/* - 23 */ {"???","???"},
/* Y 24 */ {"TAC","TAT"},
/* - 25 */ {"???","???"}
                                                    97/216
char * error_text[] = {
/* 00 */ ""
/* 01 */ ,"ERROR: Input file not found!"
/* 02 */ ,"ERROR: Memory allocation error"
/* 03 */ ,"ERROR: File read error"
/* 04 */ ,"ERROR: Could not create output file"
/* 05 */ ,"ERROR: Segment overlap must be less than segment length"
char disease_name[KEYBOARD BUFFER SIZE];
char input_file_name[KEYBOARD_BUFFER_SIZE];
char output_file_name[KEYBOARD BUFFER SIZE];
int num_genes = 0;
int num segments = 0;
int len segment;
int segment overlap;
P GENE first gene = NULL;
P_GENE SEGMENT first segment = NULL;
P_GENE_SEGMENT * scrambled_segments = NULL;
/* Mainline */
void main() {
           int error = E NOERROR;
           printf("Scramble - Version %s, %s\n\n", VERSION NO, VERSION DATE):
           /* Initial processing */
           if (!error)
                      error = prolog();
           /* Get various program parameters from user */
           if (!error)
                      error = get parameters();
           /* Load genes from genes file */
           if (!error)
                      error = load_genes();
           /* Add 'AA' to start and end of all genes */
           if (!error)
                      error = add aa();
           /* Split genes into overlapping chunks */
           if (!error)
                      error = split genes();
           /* Convert segment amino acid to dna */
           if (!error)
                      error = convert_segments aa to dna();
```

Figure 25 (Cont)

```
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             /* Scramble the segments */
            if (!error)
                        error = perform_scramble();
            /* Write output file */
            if (!error)
                        error = write_output file();
            /* Show error if there was one */
            if (error)
                        printf("%s\n",error text[error]);
}
/* prolog() */
/* Perform any initial processing required */
int prolog() {
            /* Seed the random number generator, using the system clock */
            /* Don't run the program more than once in the same second! */
            /* Or we'll get the same randomisation!!!!!!!!!!!!! */
            srand(time(NULL));
            return E_NOERROR;
}
/* get parameters() */
/* Ask for various parameters from the user (stdin) */
     Disease name
                                          */
     Input file name
     Output file name
                                          */
     Segment length
int get_parameters() {
            int valid;
           read_str("Enter disease name : ",disease_name);
read_str("Enter input file name : ",input_file_name);
           read_str("Enter output file name : ",output_file_name);
           valid = FALSE:
           while (!valid) {
                       len segment = read int("Enter segment length : ");
                       if (len segment % 2)
                                   printf("Segment length must be even!\n");
                       else
                                   valid = TRUE;
           segment_overlap = len_segment / 2;
           return E_NOERROR;
}
/* load genes() */
```

Figure 25 (Cont)

```
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/* Load the genes from the input file */
int load_genes() {
          FILE * input file;
          char name_buf[BUFFER_SIZE];
          char data buf[BUFFER_SIZE];
          int rc;
          /* Open genes file for reading */
          if (NULL == (input_file = fopen(input_file_name, "r")))
                     return E NOINFILE;
          printf("Loading genes from: %s\n",input_file_name);
          num_genes = 0;
          /* Read gene name */
          while (NULL != read_nonblank_line(name_buf,BUFFER_SIZE,input_file)) {
                     /* Read the gene data */
                     if (NULL != read_nonblank_line(data_buf,BUFFER_SIZE,input_file)) {
                                 /* Allocate memory for new gene and add to list */
                                if (rc = add gene(name_buf,data_buf))
                                            break;
                     }
           /* Close genes file */
           fclose(input file);
           return rc;
}
/* add gene() */
/* Allocate memory for new gene, then insert in list */
int add_gene(char * gene_name,char * gene_data) {
           P GENE new_gene;
           /* Allocate storage for new gene */
           if (NULL == (new_gene = malloc(sizeof(GENE))))
                      return E_MALLOC;
           /* Initialise new gene */
           new_gene->next_gene = NULL;
           /* Allocate storage for gene name (+1 for null) */
           if (NULL == (new_gene->name = malloc(strlen(gene_name)+1)))
                     return E MALLOC;
           /* Store gene name */
           strcpy(new_gene->name,gene_name);
           /* Allocate storage for gene data (+1 for null) */
           if (NULL == (new_gene->data = malloc(strlen(gene_data)+1)))
                      return E MALLOC;
           /* Store gene data */
           strcpy(new_gene->data,gene_data);
           /* Insert the new gene into linked list */
           insert gene(&first_gene,new_gene);
           /* Increment num_genes */
           num_genes++;
```

Figure 25 (Cont)

```
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          return E_NOERROR;
}
/* insert_gene() */
/* Insert gene into linked list */
void insert_gene(P_GENE * head_gene,P_GENE new_gene) {
          P_GENE * cur_ptr = head_gene;
          while (NULL != (*cur_ptr))
                     cur ptr = &((*cur ptr)->next_gene);
          *cur ptr = new gene;
}
/* add aa() */
/* Add 'AA' to the start and end of every gene */
int add_aa() {
           P_GENE cur_gene = first_gene;
          char * new_data;
          while (NULL != cur_gene) {
                     /* Allocate storage to fit the gene plus four characters */
                     new data = malloc(strlen(cur_gene->data)+5);
                     /* Shift gene data to new storage, add "AA" */
                     strcpy(new_data,"AA");
                     strcat(new_data,cur_gene->data);
                     strcat(new_data,"AA");
                     /* Free previous gene data storage */
                     free(cur_gene->data);
                     /* Set gene data pointer to new storage */
                     cur_gene->data = new_data;
                     /* Advance to next gene */
                     cur_gene = cur_gene->next_gene;
          }
          return E NOERROR;
}
/* split_genes() */
/* Split the genes into overlapping segments */
int split_genes() {
          P GENE cur gene = first_gene;
          P GENE SEGMENT cur_seg = first_segment;
          printf("Splitting genes into segments...\n");
          /* Split the genes into segments */
          while (NULL != cur_gene) {
                     /* Split the gene */
                     split_gene(cur_gene);
                     /* Advance to next gene */
```

Figure 25 (Cont)

```
cur_gene = cur_gene->next_gene;
           }
           /* Count the number of segments */
           num segments = 0;
           cur_seg = first_segment;
          while (NULL != cur_seg) {
                     num_segments++;
                     cur_seg = cur_seg->next_seg;
          }
          return E_NOERROR;
}
/* split_gene() */
/* Split a gene into overlapping segments */
int split_gene(P_GENE g) {
          char * seg_ptr;
          char * seg_buf;
          P_GENE_SEGMENT new_segment = NULL;
          int done:
          int seg ctr = 0;
          /* Allocate memory for segment buffer */
          if (NULL == (seg_buf = malloc(len_segment+1)))
                    return E_MALLOC;
         /* Insert a null at the end of the segment buffer, */
         /* so we can use it as a string */
         seg bufflen segment] = '\0':
         /* Set segment pointer to start of gene data */
         seg_ptr = g->data;
         done = FALSE;
         while (!(done)) {
                    /* So we know if we copied data */
                    seg buf[0] = '\0';
                    /* Copy a segment of gene data to the segment buffer */
                    memcpy(seg_buf,seg_ptr,len_segment);
                    /* If there was some gene data copied to the buffer */
                    if (NULL != seg_buf[0]) {
                               /* Allocate storage for a new segment */
                               if (NULL == (new_segment = malloc(sizeof(GENE SEGMENT))))
                                         return E_MALLOC;
                               /* Increment segment counter */
                               seg ctr++;
                               /* Setup the new segment */
                               new_segment->p_gene = g;
                               new_segment->number = seg ctr;
                               new_segment->offset = seg_ptr - g->data + 1;
                              new_segment->next_seg = NULL;
```

```
if (NULL == (new_segment->amino_data = malloc(len_segment+1)))
                                            return E_MALLOC;
                                 if (NULL == (new_segment->dna_data = malloc(len_segment*3+1)))
                                            return E_MALLOC;
                                 new_segment->amino_data[0] = '\0';
                                 new_segment->dna_data[0] = '\0';
                                 /* Copy segment data from buffer to new segment */
                                 strcpy(new_segment->amino_data,seg_buf);
                                 /* Insert new segment into chain from gene */
                                 insert_segment(&first_segment,new_segment);
                      /* If we didn't read a full segment, we are finished! */
                      if (strlen(seg_buf) < len_segment)
                                 done = TRUE:
                      /* Otherwise, advance segment pointer to next segment in buffer */
                      else
                                 seg_ptr = seg_ptr + len_segment - segment overlap;
           }
/* insert_segment() */
/* Insert a segment node at the end of the list */
int insert_segment(P_GENE_SEGMENT * head_seg,P_GENE_SEGMENT new_seg) {
          P_GENE_SEGMENT * cur ptr = head seg;
          while (NULL != (*cur ptr))
                     cur_ptr = &((*cur_ptr)->next_seg);
          *cur ptr = new_seg;
}
/* convert segments aa to dna */
/* Go thru segments, and for each, convert amino acids to dna */
int convert_segments_aa_to_dna() {
          P_GENE_SEGMENT cur_seg = first_segment;
          int first choice = 1:
          int alternate;
          printf("Converting to DNA...\n");
          /* Work out if we need to alternate the first codon choice or not */
          /* Don't need to do this anymore, since the segment length is
          /* forced to be even, and the overlap is half the length (odd). */
          /*alternate = ((even(len_segment) && even(segment_overlap))
                                || (!even(len_segment) && !even(segment_overlap)));*/
          alternate = FALSE;
         while (NULL != cur_seg) {
                     cur_seg->first_codon_choice = first_choice;
                     convert_aa_to_dna(cur_seg->amino_data,cur_seg->dna_data,
                                                                           cur_seg->first_codon_choice);
```

```
/* Address next segment */
                          cur_seg = cur_seg->next_seg;
                          /* If we are alternating, alternate the first codon choice */
                         /*if (alternate)
                                     if (1 == first choice)
                                                first choice = 2;
                                     else
                                                first choice = 1:*/
             }
             return E_NOERROR;
 }
 /* convert_aa_to_dna */
 /* Converts a string of amino acid to dna */
 /* NOTE: assumes that buffer at dna_ptr is large enough to hold dna!!! */
 int convert_aa_to_dna(char * aa_ptr,char * dna_ptr,int first_choice) {
            char * p_codon;
            int cur_preferred = first_choice;
            while ('\0' != *aa_ptr) {
                        p_codon = codon(*aa_ptr,cur_preferred);
                        strcat(dna_ptr,p_codon);
                        /* If we didn't find a codon, log a warning */
                        if (0 == strcmp(p_codon,"???\0"))
printf("WARNING: no codon found for amino acid!\n");
                        /* Alternate current preferred codon */
                        if (1 == cur_preferred)
                                    cur_preferred = 2;
                        else
                                    cur preferred = 1;
                        aa_ptr++;
           return E_NOERROR;
}
/* codon */
/* Returns a pointer to a codon corresponding to the amino acid passed */
/* The codon pointer is to 3 characters, plus a terminating null */
char * codon(char acid_char,int preferred) {
           int codon_table index;
           char * codon ptr;
           /* Determine index into codon_table (table starts at 'A') */
           codon_table_index = acid_char - 'A';
           /* Set pointer to appropriate codon */
           codon_ptr = codon_table[codon_table_index][preferred-1];
```

```
return codon ptr;
 }
 /* display genes() */
 /* Display the name and data for all genes */
 int display_genes() {
            P_GENE cur_gene = first_gene;
            while (NULL != cur_gene) {
                       printf("%s\n",cur_gene->name);
                       printf("%s\n",cur_gene->data);
                       cur gene = cur gene->next gene;
            }
            return E_NOERROR;
 }
 /* perform_scramble() */
 /* Scramble the segments */
 /* Check for adjacent segments. If there are, rescramble */
 int perform_scramble() {
            int done = FALSE;
           int rc = E_NOERROR;
           while (TRUE) {
                      rc = scramble segments();
                      if (E NOERROR == rc)
                                 if (adjacent_segments()) {
                                            printf("Adjacent segments detected! Rescramble? (y/n) ");
                                            if (!user_confirmation()) {
                                                       printf("WARNING: Adjacent segments in output
file.\n");
                                                       break;
                                            }
                                 else
                                            break;
                      else
                                break;
           }
           return rc;
}
/* scramble_segments() */
/* Randomly scramble the segments, putting pointers in scrambled_segments[] */
int scramble_segments() {
          P_GENE_SEGMENT cur_seg = first_segment;
          int i,j;
          P_GENE_SEGMENT temp;
          printf("Scrambling segments...\n");
```

```
/* Allocate storage for array of segment pointers */
             if (NULL == (scrambled_segments = malloc(sizeof(P GENE SEGMENT)*num segments)))
                        return E MALLOC;
            /* First, initialise scrambled_segments in same order as linked list */
            i = 0;
            while (cur_seg != NULL) {
                        scrambled_segments[i] = cur seg;
                        cur_seg = cur_seg->next_seg;
            }
            /* Now, randomly scramble the segments */
            for (i=0;i<num_segments;i++) {
                                     = rand() % num_segments;
                                       = scrambled_segments[i];
                       scrambled_segments[i] = scrambled_segments[j];
                       scrambled segments[i] = temp;
            return E_NOERROR;
}
/* adjacent_segments() */
/* Determine if the scrambled segment order has resulted in */
/* two segments which were adjacent originally (ie every
/* second one) have ended up adjacent.
int adjacent_segments() {
           int i;
           int rc = 0;
           P_GENE_SEGMENT cur_seg;
           P_GENE_SEGMENT next_seg;
           for (i=0;i<num_segments-1;i++) {
                       /* Address current and next segments */
                       cur_seg = scrambled_segments[i];
next_seg = scrambled_segments[i+1];
                       /* Do segments come from same gene, and are two apart? */
                       if (((cur_seg->p_gene == next_seg->p_gene)
                                  && ((cur_seg->number == (next_seg->number)+2)
                                            (cur_seg->number == (next_seg->number)-2))))
                                 return 1;
           return 0;
/* write_output_file() */
/* Write out segments (in initial non-scrambled order) */
/* Write out synthetic protein (in scrambled order) */
/* Write out synthetic dna (in scrambled order) */
int write_output_file() {
           FILE * output file;
```

```
char * amino buffer;
 P_GENE_SEGMENT cur seg;
 /* Open output file for writing (erase any contents) */
 if (NULL == (output_file = fopen(output_file_name,"w")))
             return E CREATE OUTPUT FILE;
 /* Allocate memory for padded amino string buffer */
 if (NULL == (amino_buffer = malloc(len_segment*3+1)))
             return E MALLOC;
 printf("Writing output file: %s\n",output_file_name);
 /* Write output file header information */
 fprintf(output file, "Scramble %s - Output File\n", VERSION_NO);
 fprintf(output file,"\n");
 fprintf(output_file,"Disease name : %s\n",disease name);
fprintf(output file,"Input filename: %s\n",input file name);
fprintf(output file,"Output filename: %s\n",output file name);
fprintf(output file,"Number genes : %d\n",num genes);
fprintf(output_file,"Number segments : %d\n",num_segments);
fprintf(output_file,"Segment length : %d\n",len_segment);
fprintf(output_file,"Segment overlap : %d\n",segment_overlap);
/* Write out segments in initial non-scrambled order */
fprintf(output_file,"\n");
fprintf(output_file,"Segments in original order:\n");
fprintf(output_file,"-----\n");
cur seg = first segment;
while (NULL != cur_seg) {
            /* Format amino data to line up with codons */
            pad_amino_string(cur_seg->amino_data,amino_buffer);
            fprintf(output_file,"Gene : %s\n",cur_seg->p_gene->name);
fprintf(output_file,"Segment# : %d\n",cur_seg->number);
            fprintf(output_file,"Offset : %d\n",cur_seg->offset);
            fprintf(output file,"1st Codon: %d\n",cur seg->first codon choice);
            fprintf(output file, "%s\n", amino buffer);
            fprintf(output_file,"%s\n",cur_seg->dna data);
            fprintf(output file,"\n");
            cur seg = cur seg->next seg;
}
/* Write out segment names in scrambled order */
fprintf(output_file,"Segments in scrambled order:\n");
fprintf(output file,"-----\n");
for (i=0;i<num segments;i++) {
            /* Format amino data to line up with codons */
            pad_amino_string(scrambled_segments[i]->amino_data,amino_buffer);
            /* Write segment details */
            fprintf(output_file,"%s #%d\n",scrambled segments[i]->p_gene->name,
                       scrambled_segments[i]->number);
           fprintf(output_file,"%s\n",amino_buffer);
fprintf(output_file,"%s\n",scrambled_segments[i]->dna_data);
            fprintf(output_file,"\n");
```

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```
/* Write synthetic protein in one long string */
              fprintf(output_file,"Synthetic Protein:\n");
fprintf(output_file,"-----\n");
              for (i=0;i<num_segments;i++)
                          fprintf(output_file, "%s", scrambled_segments[i]->amino_data);
              fprintf(output_file,"\n\n");
              /* Write synthetic dna in one long string */
             fprintf(output_file,"Synthetic DNA:\n");
fprintf(output_file,"-----\n");
             for (i=0;i<num_segments;i++)
                         fprintf(output_file, "%s", scrambled_segments[i]->dna data);
             return E_NOERROR;
 }
 /* strip newline() */
 /* Replace the first newline character with a null */
 void strip_newline(char * strip_str) {
             char * newline_pos;
             /* Find the newline char */
             newline_pos = strchr(strip str,'\n');
             /* If we found one, replace it with a null */
             if (NULL != newline_pos)
                         newline_pos[0] = '\0';
}
 /* pad amino string */
 /* Copy amino chars from amino_ptr to padded_ptr, padding each */
/* side with a space. */
void pad_amino_string(char * amino_ptr, char * padded_ptr) {
            while ('\0' != *amino_ptr) {
                         *padded_ptr = ' ';
                        padded ptr++;
                        *padded_ptr = *amino ptr;
                        padded ptr++;
                        *padded_ptr = ' ';
                        padded_ptr++;
                        amino_ptr++;
            }
            /* Stick a null at the end of the padded string */
            *padded ptr = '\0';
}
/* even() */
/* True if test num is even, otherwise false */
```

}

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```
int even(int test num) {
             return !(test num % 2);
  }
  /* read_int() */
  /* Read an integer from stdin. Keep trying until valid int > 0 entered. */
 /* Return the integer read, or 0 if error reading from stdin. */
 int read_int(char * prompt) {
             char buffer[KEYBOARD_BUFFER_SIZE];
             int value_read;
             int valid = FALSE;
            while (!valid) {
                        printf("%s",prompt);
                        valid = TRUE;
                        fgets(buffer, KEYBOARD_BUFFER SIZE, stdin);
                        if (1 != sscanf(buffer,"%d",&value_read))
                                    valid = FALSE;
                        if (valid && (value_read < 1))
                                    valid = FALSE;
                        if (!valid)
                                    printf("Positive integer value please!\n");
            }
            return value_read;
}
/* read_str() */
/* Read a string from the user (stdin) */
/* Strip the newline from it */
void read_str(char * prompt,char * string) {
           char buffer[KEYBOARD_BUFFER SIZE];
           printf(prompt);
           fgets(buffer,KEYBOARD_BUFFER SIZE,stdin);
           sscanf(buffer, "%s", string);
}
/* read_nonblank_line() */
/* Read a line from file until we get a non-blank one */
char * read_nonblank_line(char * buf,int buf_size,FILE * in file) {
           char * return_ptr;
          /* Read lines until we get a non-black one, or EOF */
          do
                      return_ptr = fgets(buf,buf_size,in_file);
          while ((NULL != return_ptr) && (('\n' == buf[0]) || (' ' == buf[0])));
          /* If we got a line, change the newline char to a null */
          if (NULL != return_ptr)
                      strip_newline(buf);
```

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```
return return_ptr;
 /* user_confirmation() */
 /* Read input from user. If user types 'y', return 1, otherwise 0 */
 int user_confirmation() {
                 char buffer[KEYBOARD_BUFFER_SIZE];
                 fgets(buffer,KEYBOARD_BUFFER_SIZE,stdin);
                 if (('y' == buffer[0]) || ('Y' == buffer[0]))
                                return 1;
                 else
                                return 0;
}
/* test() */
/* For debugging/development */
void test() {
               {
    char str[100];
    printf("Enter something: ");
    fgets(str,100,stdin);
    printf("line1\n");
    printf("%s",str);
    printf("line2\n");
    fgets(str,100,stdin);
}
```

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HepC Savine design

HepC la consensus polyprotein sequence used for scramble program

MSTNPKPQRKTKRNTNRRPQDVKFPGGGQIVGGVYLLPRRGPRLGVRATRKTSERSQPRGRRQPIPKARRPEGRTWAO PGYPWPLYGNEGCGWAGWLLSPRGSRPSWGPTDPRRRSRNLGKVIDTLTCGFADLMGYIPLVGAPLGGAARALAHGVR VLEDGVNYATGNLPGCSFSIFLLALLSCLTVPASAYQVRNSTGLYHVTNDCPNSSIVYEAADAILHTPGCVPCVREGN ASRCWVAMTPTVATRDGKLPATQLRRHIDLLVGSATLCSALYVGDLCGSVFLVGQLFTFSPRRHWTTQGCNCSIYPGH ITGHRMAWDMMNWSPTAALVMAQLLRIPQAILDMIAGAHWGVLAGIAYFSMVGNWAKVLVVLLLFAGVDAETHVTGG ${\tt NAGRTTSGLVSLLTPGAKQNIQLINTNGSWHINSTALNCNESLNTGWLAGLFYQHKFNSSGCPERLASCRRLTDFDQG}$ WGPISYANGSGPDQRPYCWHYPPKPCGIVPAKSVCGPVYCFTPSPVVVGTTDRSGAPTYSWGANDTDVFVLNNTRPPL GNWFGCTWMNSTGFTKVCGAPPCVIGGAGNNTLHCPTDCFRKHPEATYSRCGSGPWITPRCLVDYPYRLWHYPCTINY TIFKVRMYVGGVEHRLEAACNWTRGERCDLEDRDRSELSPLLLSTTQWQVLPCSFTTLPALSTGLIHLHQNIVDVQYL YGVGSSIASWAIKWEYVVLLFLLLADARVCSCLWMMLLISQAEAALENLVILNAASLAGTHGLVSFLVFFCFAWYLKG ${\tt RWVPGAVYALYGMWPLLLLLLALPQRAYALDTEVAASCGGVVLVGLMALTLSPYYKRYISWCLWWLQYFLTRVEAQLH}$ ${\tt VWVPPLNVRGGRDAVILLMCVVHPTLVFDITKLLLAVFGPLWILQASLLKVPYFVRVQGLLRICALARKMIGGHYVQM}$ AIIKLGALTGTYVYNHLTPLRDWAHNGLRDLAVAVEPVVFSQMETKLITWGADTAACGDIINGLPVSARRGREILLGP ADGMVSKGWRLLAPITAYAQQTRGLLGCIITSLTGRDKNQVEGEVQIVSTAAQTFLATCINGVCWTVYHGAGTRTIAS PKGPVIQMYTNVDQDLVGWPAPQGSRSLTPCTCGSSDLYLVTRHADVIPVRRRGDSRGSLLSPRPISYLKGSSGGPLL CPAGHAVGIFRAAVCTRGVAKAVDFIPVENLETTMRSPVFTDNSSPPAVPQSFQVAHLHAPTGSGKSTKVPAAYAAQG YKVLVLNPSVAATLGFGAYMSKAHGIDPNIRTGVRTITTGSPITYSTYGKFLADGGCSGGAYDIIICDECHSTDATSI ${\tt LGIGTVLDQAETAGARLVVLATATPPGSVTVPHPNIEEVALSTTGEIPFYGKAIPLEVIKGGRHLIFCHSKKKCDELA}$ ${ t AKLVALGINAVAYYRGLDVSVIPTSGDVVVVATDALMTGYTGDFDSVIDCNTCVTQTVDFSLDPTFTIETTTLPQDAV$ SRTQRRGRTGRGKPGIYRFVAPGERPSGMFDSSVLCECYDAGCAWYELTPAETTVRLRAYMNTPGLPVCQDHLEFWEG VFTGLTHIDAHFLSQTKQSGENFPYLVAYQATVCARAQAPPPSWDQMWKCLIRLKPTLHGPTPLLYRLGAVQNEVTLT HPVTKYIMTCMSADLEVVTSTWVLVGGVLAALAAYCLSTGCVVIVGRIVLSGKPAIIPDREVLYREFDEMEECSQHLP YIEQGMMLAEQFKQKALGLLQTASRQAEVIAPAVQTNWQKLEVFWAKHMWNFISGIQYLAGLSTLPGNPAIASLMAFT AAVTSPLTTSQTLLFNILGGWVAAQLAAPGAATAFVGAGLAGAAIGSVGLGKVLVDILAGYGAGVAGALVAFKIMSGE VPSTEDLVNLLPAILSPGALVVGVVCAAILRRHVGPGEGAVQWMNRLIAFASRGNHVSPTHYVPESDAAARVTAILSS LTVTQLLRRLHQWISSECTTPCSGSWLRDIWDWICEVLSDFKTWLKAKLMPQLPGIPFVSCQRGYKGVWRGDGIMHTR CHCGAEITGHVKNGTMRIVGPRTCRNMWSGTFPINAYTTGPCTPLPAPNYTFALWRVSAEEYVEIRRVGDFHYVTGMT TDNLKCPCQVPSPEFFTELDGVRLHRFAPPCKPLLREEVSFRVGLHEYPVGSQLPCEPEPDVAVLTSMLTDPSHITAE ${\tt AAGRRLARGSPPSMASSSASQLSAPSLKATCTANHDSPDAELIEANLLWRQEMGGNITRVESENKVVILDSFDPLVAE}$ EDEREISVPAEILRKSRRFAQALPVWARPDYNPPLVETWKKPDYEPPVVHGCPLPPPRSPPVPPPRKKRTVVLTESTL STALAELATKSFGSSSTSGITGDNTTTSSEPAPSGCPPDSDAESYSSMPPLEGEPGDPDLSDGSWSTVSSEAGTEDVV CCSMSYSWTGALVTPCAAEEQKLPINALSNSLLRHHNLVYSTTSRSACQRQKKVTFDRLOVLDSHYODVLKEVKAAAS KVKANLLSVEEACSLTPPHSAKSKFGYGAKDVRCHARKAVAHINSVWKDLLEDSVTPIDTTIMAKNEVFCVQPEKGGR ${\tt KPARLIVFPDLGVRVCEKMALYDVVSKLPLAVMGSSYGFQYSPGQRVEFLVQAWKSKKTPMGFSYDTRCFDSTVTESD}$ $\tt IRTEEAIYQCCDLDPQARVAIKSLTERLYVGGPLTNSRGENCGYRRCRASGVLTTSCGNTLTCYIKARAACRAAGLQD$ ${\tt CTMLVCGDDLVVICESAGVQEDAASLRAFTEAMTRYSAPPGDPPQPEYDLELITSCSSNVSVAHDGAGKRVYYLTRDP}$ TTPLARAAWETARHTPVNSWLGNIIMFAPTLWARMILMTHFFSVLIARDQLEQALDCEIYGACYSIEPLDLPPIIORL HGLSAFSLHSYSPGEINRVAACLRKLGVPPLRAWRHRARSVRARLLARGGRAAICGKYLFNWAVRTKLKLTPIAAAGR LDLSGWFTAGYSGGDIYHSVSHARPRWFWFCLLLLAAGVGIYLLPNR

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Scramble - Output File
Scramble version: 0.1 beta, 08/02/1999
Num. genes
              : 1
               : 201
Num. segments
Segment length
Segment overlap : 15
Segments in original order:
         : HepCla
Gene
Segment#
        : 1
Offset
1st Codon : 1
A A M S T N P K P Q R K T K R N T N R R P Q D V K F P G G G
GCCGCTATGTCCACCAATCCCAAACCCCAAAGGAAAACCAAAAGGAATACCAATAGGAGACCCCAAGACGTCAAGTTTCCCGGAGGCGGA
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111/216 Gene : HepCla Segment# : 2 Offset : 16 1st Codon : 1 NTNRRPQDVKFPGGGQIVGGVYLLPRRGPR AACACAAACAGAAGGCCTCAGGATGTGAAATTCCCTGGCGGAGGCCAAATCGTCGGCGGAGTGTATCTGCTCCCCAGAAGGGGACCCAGA Gene : HepCla Segment# : 3 Offset : 31 1st Codon : 1 Q I V G G V Y L L P R R G P R L G V R A T R K T S E R S Q P Gene : HepCla Segment# : 4 Offset : 46 1st Codon : 1 LGVRATRKTSERSQPRGRRQPIPKAR_{PEG} Gene : HepCla Segment# : 5 Offset : 61 1st Codon : 1 R G R R Q P I P K A R R P E G R T W A Q P G Y P W P L Y G N AGGGGAAGGACACCTATCCCTAAGGCTAGGAGACCCGAAGGCAGAACCTGGGCCCAACCCGGATACCCTTGGCCTCTGTATGGCAAT: HepCla Segment# : 6 Offset : 76 1st Codon : 1 R T W A Q P G Y P W P L Y G N E G C G W A G W L L S P R G S AGGACATGGGCTCAGCCTGGCTATCCCTGGCCCCTCTACGGAAACGAAGGCTGTGGCTGGGCCGGATGGCTCCTGTCCCCCAGAGGCTCC Gene : HepCla Segment# : 7 Offset : 91 E G C G W A G W L L S P R G S R P S W G P T D P R R S R N ${\tt GAGGGATGCGGATGGCTGGCTGGCTCAGCCCTAGGGGAAGCAGACCCTCCTGGGGACCCACAGACCCTAGGAGAAGGTCCAGGAAT}$: HepCla Segment# : 8 Offset : 106 1st Codon : 1 R P S W G P T D P R R R S R N L G K V I D T L T C G F A D L ${\tt AGGCCTAGCTGGGGCCCTACCGATCCCAGAAGGAGAAGCAGAAACCTCGGCAAAGTGATTGACACACTGACATGCGGATTCGCTGACCTC}$ Gene : HepCla Segment# : 9 Offset : 121 1st Codon : 1 LGKVIDTLTCGFADLMGYIPLVGAPLGGAA : HepCla Gene Segment# : 10 Offset : 136 1st Codon : 1

M G Y I P L V G A P L G G A A R A L A H G V R V L E D G V N $\tt ATGGGATACATTCCCCTCGTGGGAGCCCCTCTGGGAGGCCCTGGCAGAGCCCCTCGCCCATGGCGTCAGGGTCCTGGAAGACGGAGTGAAT$

Gene : HepCla : 11 Segment# Offset : 151 1st Codon : 1

AGGGCTCTGGCTCACGGAGTGAGAGTGCTCGAGGATGGCGTCAACTATGCCACAGGCAATCTGCCTGGCTGTAGCTTTAGCATTTTCCTC

Gene : HepCla Segment# : 12 Offset : 166

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1st Codon : 1 Y A T G N L P G C S F S I F L L A L L S C L T V P A S A Y Q TACGCTACCGGAAACCTCCCCGGATGCTCCTTCTCCATCTTTCTGCTCGCCCTCCTGTCCTGCCTCACCGTCCCCGCTAGCGCTTACCAA Gene : HepCla Segment# : 13 Offset : 181 1st Codon : 1 L A L L S C L T V P A S A Y Q V R N S T G L Y H V T N D C P $\tt CTGGCTCTGGCTGACCAGTGCCTGCCTCCGCCTATCAGGTCAGGAATAGCACAGGCCTCTACCATGTGACAAACGATTGCCCT$: HepCla Segment# : 14 Offset : 196 V R N S T G L Y H V T N D C P N S S I V Y E A A D A I L H T $\tt GTGAGAAACTCCACCGGACTGTATCACGTCACCAATGACTGTCCCAATAGCTCCATCGTCTACGAAGCCGCTGACGCTATCCTCCACACA$: HepCla Segment# : 15 Offset : 211 1st Codon : 1 N S S I V Y E A A D A I L H T P G C V P C V R E G N A S R C AACTCCAGCATTGTGTATGAGGCTGCCGATGCCATTCTGCATACCCCTGGCTGTGTGCCTTGCGTCAGGGAAGGCAATGCCTCCAGGTGT Gene : HepCla Segment# : 16 Offset : 226 P G C V P C V R E G N A S R C W V A M T P T V A T R D G K L $\tt CCCGGATGCGTCCCCTGTGTGAGAGAGGGAAACGCTAGCAGATGCTGGGTGGCTATGACACCCACAGTGGCTACCAGAGACGGAAAGCTC$: HepCla Segment# : 17 Offset : 241 1st Codon : 1 W V A M T P T V A T R D G K L P A T Q L R R H I D L L V G S Gene : HepCla Segment# : 18 Offset : 256 1st Codon : 1 PATQLRRHIDLLVGSALLYVGDLCGS Segment# : 19 Offset : 271 1st Codon : 1 GCCACACTGTGTAGCGCTCTGTATGTGGGAGACCTCTGCGGAAGCGTCTTCCTCGTGGGACAGCTCTTCACATTCTCCCCCAGAAGGCAT Gene : HepCla Segment# : 20 : 286 Offset 1st Codon: 1 V F L V G Q L F T F S P R R H W T T Q G C N C S I Y P G H I GTGTTTCTGGTCGGCCAACTGTTTACCTTTAGCCCTAGGAGACACTGGACCACACACGGGATGCAATTGCTCCATCTATCCCGGACACATT : HepCla Segment# : 21 Offset : 301 W T T Q G C N C S I Y P G H I T G H R M A W D M M M N W S P $\tt TGGACAACCCAAGGCTGTAACTGTAGCATTTACCCTGGCCATATCACAGGCCATAGGATGGCCTGGGACATGATGATGAACTGGAGCCCT$ Gene : HepCla Segment# : 22 Offset : 316 1st Codon : 1 T G H R M A W D M M M N W S P T A A L V M A Q L L R I P Q A ACCGGACACAGAATGGCTTGGGATATGATGATGATTGGTCCCCCACAGCCGCTCTGGTCATGGCTCAGGCTCCTGAGAATCCCTCAGGCT

Figure 26 (Cont)

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: HepCla Segment# : 23 Offset : 331 1st Codon : 1 T A A L V M A Q L L R I P Q A I L D M I A G A H W G V L A G $\verb|ACCGCTGCCCTCGTGATGGCCCAACTGCTCAGGATTCCCCAAGCCATTCTGGATATGATTGCCGGAGCCCATTGGGGAGTGCTCGCCGGA$: HepCla Segment# : 24 Offset : 346 1st Codon : 1 I L D M I A G A H W G V L A G I A Y F S M V G N W A K V L V Gene : HepCla Segment# : 25 : 361 Offset 1st Codon : 1 I A Y F S M V G N W A K V L V V L L L F A G V D A E T H V T ATCGCTTACTTTAGCATGGTGGGAAACTGGGCCAAAGTGCTCGTGGTCCTGCTCTGTTTGCCGGAGTGGATGCCGAAACCCATGTGACA : HepCla Segment# : 26 Offset : 376 1st Codon : 1 V L L F A G V D A E T H V T G G N A G R T T S G L V S L L GTGCTCCTGCTCTCGCTGGCGTCGACGCTGACACACGTCACCGGAGGCAATGCCGGAAGGACAACCTCCGGCCTCGTGTCCCTGCTC Gene : HepCla Segment# : 27 Offset : 391 1st Codon : 1 G G N A G R T T S G L V S L L T P G A K Q N I Q L I N T N G GGCGGAAACGCTGGCAGAACCACAAGCGGACTGGTCAGCCTCCTGACACCCGGAGCCAAACAGAATATCCAACTGATTAACACAAACGGA : HepCla Gene Segment# : 28 Offset : 406 1st Codon : 1 T P G A K Q N I Q L I N T N G S W H I N S T A L N C N E S L ACCCCTGGCGCTAAGCAAAACATTCAGCTCATCAATACCAATGGCTCCTGGCATATCAATAGCACAGCCCTCAACTGTAACGAAAGCCTC Gene : HepCla Segment# : 29 : 421 1st Codon : 1 S W H I N S T A L N C N E S L N T G W L A G L F Y Q H K F N AGCTGGCACATTAACTCCACCGCTCTGAATTGCAATGAGTCCCTGAATACCGGATGGCTCGCCGGACTGTTTTACCAACACAAATTCAAT : HepCla Segment# : 30 Offset. : 436 1st Codon : 1 N T G W L A G L F Y Q H K F N S S G C P E R L A S C R R L T AACACAGGCTGGCTGGCCTCTTCTATCAGCATAAGTTTAACTCCAGCGGATGCCCTGAGAGACTGGCTAGCTGTAGGAGACTGACA Gene : HepCla Segment# : 31 Offset : 451 1st Codon : 1 $\mathtt{S} \quad \mathtt{S} \quad \mathtt{G} \quad \mathtt{C} \quad \mathtt{P} \quad \mathtt{E} \quad \mathtt{R} \quad \mathtt{L} \quad \mathtt{A} \quad \mathtt{S} \quad \mathtt{C} \quad \mathtt{R} \quad \mathtt{R} \quad \mathtt{L} \quad \mathtt{T} \quad \mathtt{D} \quad \mathtt{F} \quad \mathtt{D} \quad \mathtt{Q} \quad \mathtt{G} \quad \mathtt{W} \quad \mathtt{G} \quad \mathtt{P} \quad \mathtt{I} \quad \mathtt{S} \quad \mathtt{Y} \quad \mathtt{A} \quad \mathtt{N} \quad \mathtt{G} \quad \mathtt{S}$ AGCTCCGGCTGTCCCGAAAGGCTCGCCTCCTGCAGAAGGCTCACCGATTTCGATCAGGGATGGGGACCCATTAGCTATGCCAATGGCTCC : HepCla Gene Segment# : 32 Offset : 466 1st Codon : 1 D F D Q G W G P I S Y A N G S G P D Q R P Y C W H Y P P K P

Gene : HepCla Segment# : 33

GACTTTGACCAAGGCTGGGGCCCTATCTCCTACGCTAACGGAAGCGGACCCGATCAGAGACCCTATTGCTGGCACTATCCCCCTAAGCCT

114/216 Offset : 481 1st Codon : 1 G P D Q R P Y C W H Y P P K P C G I V P A K S V C G P V Y C GGCCCTGACCAAAGGCCTTACTGTTGGCATTACCCTCCCAAACCCTGTGGCATTGTGCCTACAAAAGCGTCTGCGGACCCGTCTACTGT : HepCla Segment# : 34 Offset : 496 1st Codon : 1 C G I V P A K S V C G P V Y C F T P S P V V V G T T D R S G Gene : HepCla Segment# : 35 Offset : 511 1st Codon : 1 FTPSPVVVGTTDRSGAPTYSWGANDTDVFV Gene : HepCla Segment# : 36 Offset : 526 1st Codon : 1 A P T Y S W G A N D T D V F V L N N T R P P L G N W F G C T GCCCCTACCTATAGCTGGGGCGCTAACGATACCGATGTGTTTTGTGCTCAACAATACCAGACCCCCTCTGGGAAACTGGTTCGGATGCACA : HepCla Segment# : 37 Offset: : 541 1st Codon : 1 LNNTRPPLGNWFGCTWMNSTGFTKVCGAPP $\tt CTGAATAACACAAGGCCTCCCCTCGGCAATTGGTTTGGCTGTACCTGGATGAATAGCACAGGCTTTACCAAAGTGTGTGGCGCTCCCCCT$ Gene : HepCla Segment# : 38 Offset 1st Codon: 1 W M N S T G F T K V C G A P P C V I G G A G N N T L H C P T : HepCla Segment# : 39 Offset : 571 1st Codon : 1 C V I G G A G N N T L H C P T D C F R K H P E A T Y S R C G $\tt TGCGTCATCGGAGGCGCTGGCAATAACACACTGCATTGCCCTACCGATTGCTTTAGGAAACACCCTGAGGCTACCTATAGCAGATGCGGA$ Gene : HepCla Segment# : 40 Offset : 586 1st Codon : 1 D C F R K H P E A T Y S R C G S G P W I T P R C L V D Y P Y GACTGTTTCAGAAAGCATCCCGAAGCCACATACTCCAGGTGTGGCTCCGGCCCTTGGATTACCCCTAGGTGTCTGGTCGACTATCCCTAT Gene : HepCla Segment# : 41 Offset : 601 1st Codon : 1 S G P W I T P R C L V D Y P Y R L W H Y P C T I N Y T I F K AGCGGACCCTGGATCACACCCAGATGCCTCGTGGATTACCCTTACAGACTGTGGCACTATCCCTGTACCATTAACTATACCATTTCAAA Gene : HepCla Segment# : 42 Offset : 616 1st Codon : 1 R L W H Y P C T I N Y T I F K V R M Y V G G V E H R L E A A Gene : HepCla Segment# : 43

V R M Y V G G V E H R L E A A C N W T R G E R C D L E D R D

Offset

1st Codon : 1

: 631

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 $\tt GTGAGAATGTATGTGGGAGGCGTCGAGCATAGGCTCGAGGCTGCCTGTAACTGGACCAGAGGCGAAAGGTGTGACCTCGAGGATAGGGAT$

Gene : HepCla Segment# : 44 Offset : 646 1st Codon : 1

C N W T R G E R C D L E D R D R S E L S P L L L S T T Q W Q TGCAATTGGACAAGGGGACTGTGGCAAGGAGAGAGAGCGAACTGTCCCCCCTCCTGCTCAGCACAACCCAATGGCAA

Gene : HepCla
Segment# : 45
Offset : 661
1st Codon : 1

Gene : HepCla
Segment# : 46
Offset : 676
1st Codon : 1

Gene : HepCla Segment# : 47 Offset : 691 1st Codon : 1

L I H L H Q N I V D V Q Y L Y G V G S S I A S W A I K W E Y CTGATTCACCTCCACCAAAACATTGTGGATGTGCAATACCTCTACGGAGTGGGAAGCTCCATCGCTAGCTGGGCCATTAAGTGGGAGTAT

Gene : HepCla
Segment# : 48
Offset : 706
lst Codon : 1

G V G S S I A S W A I K W E Y V V L L F L L A D A R V C S GGCGTCGGCTCCAGCATTGCCTCCTGGCTATCAAATGGGAATACGTCGTGCTCCTGTTCTGCTCCTGGCTGACGCTAGGGTCTGCTCC

Gene : HepCla Segment# : 49 Offset : 721 1st Codon : 1

Gene : HepCla Segment# : 50 Offset : 736 1st Codon : 1

C L W M M L L I S Q A E A A L E N L V I L N A A S L A G T H TGCCTCTGGATGATGCTCCTGATTAGCCAAGCCGAAGCCGTCTGGAAAACCTCGTGATTCTGAATGCCGCTAGCCTCGCCGGAACCCAT

Gene : HepCla Segment# : 51 Offset : 751 1st Codon : 1

ENLVILNAASLAG THGLVSFLVFFCFAWYL

Gene : HepCla Segment# : 52 Offset : 766 lst Codon : 1

G L V S F L V F F C F A W Y L K G R W V P G A V Y A L Y G M GGCCTCGTGTCCTCCTCGTGTTTTCTGTTTCGCTTGGTATCTGAAAGGCAGATGGGTCCCCGGAGCCGTCTACGCTCTGTATGGCATG

Gene : HepCla Segment# : 53 Offset : 781 1st Codon : 1

K G R W V P G A V Y A L Y G M W P L L L L L A L P $\mathbb Q$ R A Y AAGGGAAGGTGGGTGCCTGCTGTGTGTGTGTCCTCTGCGCAATGTGGCCCTCCTGCTCCTGCTCTGGCTCTGGCTCTGAGAGAGCCTAT

Gene : HepCla

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Segment# : 54 : 796 1st Codon : 1 W P L L L L L A L P Q R A Y A L D T E V A A S C G G V V L : HepCla Segment# : 55 Offset : 811 A L D T E V A A S C G G V V L V G L M A L T L S P Y Y K R Y GCCCTCGACACAGAGGTCGCCGCTAGCTGTGGCGGAGTGGTCCTGGTCGGCCTCATGGCTCTGACACTGTCCCCCTATTACAAAAGGTAT : HepCla Segment# : 56 Offset : 826 1st Codon : 1 V G L M A L T L S P Y Y K R Y I S W C L W W L Q Y F L T R V $\tt GTGGGACTGATGGCCCTCACCCTCAGCCCTTACTATAAGAGATACATTAGCTGGTGCCTCTGGTGGCTGCAATACTTTCTGACAAGGGTC$ Gene : HepCla Segment# : 57 Offset : 841 lst Codon: 1 ISWCLWWLQYFLTRVEAQLHVWVPPLNVRG ATCTCCTGGTGTCTGTGGTGGCTCCAGTATTTCCTCACCAGAGTGGAAGCCCAACTGCATGTGTGGGTGCCTCCCCTCAACGTCAGGGGA : HepCla Segment# : 58 Offset : 856 1st Codon : 1 E A Q L H V W V P P L N V R G G R D A V I L L M C V V H P T GAGGCTCAGCTCCACGTCTGGGTCCCCCCTCTGAATGTGAGAGGCGGAAGGGATGCCGTCATCCTCGTGATGTGCGTCGTGCATCCCACA Gene : HepCla Segment# : 59 Offset : 871 1st Codon : 1 G R D A V I L L M C V V H P T L V F D I T K L L L A V F G P ' GGCAGAGACGCTGTGATTCTGCTCATGTGTGTGTGTCCACCCTACCCTCGTGTTTGACATTACCAAACTGCTCCTGGCTGTTTTGGCCCT Gene : HepCla Segment# : 60 Offset : 886 1st Codon : 1 L V F D I T K L L L A V F G P L W I L Q A S L L K V P Y F V $\tt CTGGTCTTCGATATCACAAAGCTCCTGCTCGCCGTCTTCGGACCCCTCTGGATTCTGCAAGGCCTCCCTGCTCAAGGTCCCCTATTTCGTC$ Gene : HepCla Segment# : 61 1st Codon: 1
L W I L Q A S L L K V P Y F V R V Q G L L R I C A L A R K M
L W I L Q A S L L K V P Y F V R V Q G L L R I C A L A R K M CTGTGGATCCTCCAGGCTAGCCTCCTGAAAGTGCCTTACTTTGTGAGAGTGCAAGGCCTCCTGAGAATCTGTGCCCTCGCCAGAAAGATG : HepCla Segment# : 62 Offset : 916 1st Codon : 1 R V Q G L L R I C A L A R K M I G G H Y V Q M A I I K L G A : HepCla Segment# : 63 Offset : 931 1st Codon : 1 I G G H Y V Q M A I I K L G A L T G T Y V Y N H L T P L R D $\hbox{\tt ATCGGAGGCCATTACGTCCAGATGGCCATTATCAAACTGGGAGCCCTCACCGGAACCTATGTGTATAACCATCTGACACCCCTCAGGGAT}$

Gene : HepCla Segment# : 64 Offset : 946 1st Codon : 1

117/216

L T G T Y V Y N H L T P L R D W A H N G L R D L A V A V E P : HepCla Segment# : 65 Offset : 961 1st Codon : 1 W A H N G L R D L A V A V E P V V F S Q M E T K L I T W G A TGGGCTCACAATGGCCTCAGGGATCTGGCTGTGGCTGTGGAACCCGTCGTGTTTAGCCAAATGGAAACCAAACTGATTACCTGGGGCGCT : HepCla Segment# : 66 Offset. : 976 1st Codon : 1 V V F S Q M E T K L I T W G A D T A A C G D I I N G L P V S GTGGTCTTCTCCCAGATGGAGACAAAGCTCATCACATGGGGAGCCGATACCGCTGCCTGTGGCGATATCATTAACGGACTGCCTGTGTCC Gene : HepCla Segment# : 67 Offset : 991 1st Codon : 1 D T A A C G D I I N G L P V S A R R G R E I L L G P A D G M : HepCla Segment# : 68 Offset : 1006 1st Codon : 1 ARRGREILLGPADGMVSKGWRLLAPITAYA ${\tt GCCAGAAGGGGAAATCCTCCTGGGACCGGTGACGGAATGGTCAGCAAAGGCTGGAGGCTCCTGGCTCCCATTACCGCTTACGCT}$ Gene : HepCla Segment# : 69 : 1021 V S K G W R L L A P I T A Y A Q Q T R G L L G C I I T S L T GTGTCCAAGGGATGGAGACTGCTCGCCCCTATCACAGCCTATGCCCCAACAGACAAGGGGACTGCTCGGCTGTATCATTACCTCCCTGACA : HepCla Segment# : 70 Offset : 1036 1st Codon : 1 Q Q T R G L L G C I I T S L T G R D K N Q V E G E V Q I V S CAGCAAACCAGAGGCCTCCTGGGATGCATTATCACAAGCCTCACCGGAAGGGATAAGAATCAGGTCGAGGGAGAGGTCCAGATTGTGTCC Gene : HepCla Segment# : 71 Offset : 1051 1st Codon : 1 G R D K N Q V E G E V Q I V S T A A Q T F L A T C I N G V C ${\tt GGCAGAGACAAAAACCAAGTGGAAGTGCAAATCGTCAGCACAGCCGCTCAGACATTCCTCGCCACATGCATTAACGGAGTGTGT}$: HepCla Segment# : 72 Offset : 1066 1st Codon : 1 TAAQTFLATCING V C W T V Y H G A G T R T I A S P ${\tt ACCGCTGCCCAAACCTTTCTGGCTACCTGTATCAATGGCGTCTGCTGGACCGTCTACCATGGCGCTGGCACAAGGACAATCGCTAGCCCT}$ Gene : HepCla Segment# : 73 Offset : 1081 1st Codon : 1 W T V Y H G A G T R T I A S P K G P V I Q M Y T N V D O D L TGGACAGTGTATCACGGAGCCGGAACCAGAACCATTGCCTCCCCCAAAGGCCCTGTGATTCAGATGTACACAAACGTCGACCAAGACCTC Gene : HepCla Segment# : 74 : 1096 Offset 1st Codon : 1 K G P V I Q M Y T N V D Q D L V G W P A P Q G S R S L T P C ${\tt AAGGGACCCGTCATCCAAATGTATACCAATGTGGATCAGGATCTGGTCGGCTGGCCCGCTCCCCAAGGCTCCAGGTCCCTGACACCCTGTCCCCCAAGGCTCCCAAGGCTCCCAAGGCTCCCAAGGCTCCCCAAGGCTCCCCAAGGCTCCCCAAGGCTCCCCTGACACCCCTGTCACACCCCTGTCACACCCCTGTCAAGGCTCCCAAGGCTCCCAAGGCTCCCCAAGGCTCCCCAAGGCTCCCCAAGGCTCCCCTGACACCCCTGTCAAGGCTCCCCAAGGCTCCCAAGGCTCCCCAAGGCTCCCCTGACACCCCTGTCAAGGCTCCCCAAGGCTCCCCAAGGCTCCCCTGACACCCCTGTCAAGGCTCCCCAAGGCTCCCCAAGGCTCCCCTGACACCCCTGTCAAGGCTCCCCAAGGCTCCCCAAGGCTCCCCTGACACCCCTGTCAAGGCTCCCCTGACACCCCTGTCAAGGCTCCCAAGGCTCCCAAGGCTCCCCTGACACCCCTGTCAAGGCTCCCAAGGCTCCCCAAGGCTCCCCTGACACCCCTGTCAAGGCTCCCAAGGCTCCCAAGGCTCCCAAGGCTCCCCTGACACCCCTGTCAAGGCTCCCAAGGCTCCCAAGGCTCCCAAGGCTCCCCTGACACCCCTGTCAAGGCTCCCAAGGCTCCCAAGGCTCCCAAGGCTCCCAAGGCTCCCAAGGCTCCCAAGGCTCCCCTGACACCCCTGTCAAGGCTCCCAAGGCTCCCAAGGCTCCCAAGGCTCCCAAGGCTCCCAAGGCTCCCCAAGGCTCCCCAAGGCTCCCCAAGGCTCCCCAAGGCTCCCCAAGGCTCCCCAAGGCTCCCCAAGGCTCCCCAAGGCTCCCCAAGGCTCCCCAAGGCTCCCCAAGGCTCCCCCAAGGCTCCCCCAAGGCTCCCCAAGGCTCCCCAAGGCTCCCCAAGGCTCCCCAAGGCTCCCCAAGGCTCCCCAAGGCTCCCCAAGGCTCCCCAAGGCTCCCCAAGGCTCCCCAAGGCTCCCCAAGGCTCCCCAAGGCTCCCCAAGGCTCCCCAAGGCTCCCCAAGGCTCCCCAAGGCTCCCCAAGGCTCCCCAAGGCTCCAAGGCTCCAAGGCTCCAAGGCTCCAAGGCTCCAAGGCTCCAAGGCTCAAGGCTCCAAGGCTCCAAGGCTCCAAGGCTCCAAGGCTCCAAGGCTCCAAGGCTCCAAGGCTCCAAGGCTCCAAGGCTCCAAGGCTCCAAGGCTCCAAGGCTCAAGGCTCAAGGCTCCAAGGCTCAAGGCAAGGCTCAAGGCTCAAGGCTCAAGGCTCAAGGCTCAAGGCTCAAGGCTCAAGGCTCAAGGCTCAAGGCTCAAGGCTCAAGGCTCAAGGCTCAAGGCTAAGGCAAGGCTCAAGGCTCAAGGCTCAAGGCAAGGCTCAAGGCTCAAGGCTCAAGGCTCAAGGCTCAAGGCTCAAGGCTCAAGGCTCAAGGCTCAA$

118/216

Gene : HepCla Segment# : 75 Offset : 1111 1st Codon : 1

Gene : HepCla
Segment# : 76
Offset : 1126
lst Codon : 1

T C G S S D L Y L V T R H A D V I P V R R R G D S R G S L L ACCTGTGGCTCCAGCGATCTCTGTATCTGGTCACCAGACACGCTGACGTCATCCCTGTGAGAAGGAGAGGCGATAGCAGAGGCTCCCTGCTC

Gene : HepCla
Segment# : 77
Offset : 1141
1st Codon : 1

Gene : HepCla Segment# : 78 Offset : 1156 lst Codon : 1

S P R P I S Y L K G S S G G P L L C P A G H A V G I F R A A AGCCCTAGGCCTATCTCCTACCTCAAGGGAAGCTCCGGCGGACCCCTCCTGTGTCCCGCTGGCCATGCCGTCGGCATTTTCAGAGCCGCT

Gene : HepCla Segment# : 79 Offset : 1171 1st Codon : 1

Gene : HepCla Segment# : 80 Offset : 1186 1st Codon : 1

V C T R G V A K A V D F I P V E N L E T T M R S P V F T D N GTGTGTACCAGAGGGGTCGCCAAAGCCGTCGACTTTATCCCTGTGGAAAACCTCGAGACAACCATGAGGTCCCCCGTCTTCACAGACAAT

Gene : HepCla Segment# : 81 Offset : 1201 1st Codon : 1

E N L E T T M R S P V F T D N S S P P A V P Q S F Q V A H L GAGAATCTGGAAACCACAATGAGAAGCCCTGTGTTTACCGATAACTCCAGCCCTCCCGCTGTGCCTCAGTCCTTCCAAGTGGCTCACCTC

Gene : HepCla Segment# : 82 Offset : 1216 lst Codon : 1

Gene : HepCla Segment# : 83 Offset : 1231 1st Codon : 1

HAPTGSGKSTKVPAAYAAQGYKVLVLNPSVCACGCTCCCACAGGCTACCACAGGCTCCCACAGGCTCCCACAGGCTCCCACAAAGCCACAAAGCTCCCCACCCTAGCCCTCTATGCCCTCTCAGGGATACAAAGTGCTCGTGCTCAACCCTAGCGTC

Gene : HepCla
Segment# : 84
Offset : 1246
1st Codon : 1

Y A A Q G Y K V L V L N P S V A A T L G F G A Y M S K A H G TACGCTGCCCAAGGCTATAAGGTCCTGGAATCCCTCCGTGGCTGCCACACTGGGATCCGAGCCTATATGTCCAAGGCTCACGGA

Gene : HepCla Segment# : 85 Offset : 1261

119/216

1st Codon : 1 A A T L G F G A Y M S K A H G I D P N I R T G V R T I T T G GCCGCTACCCTCGGCTTTGGCGCTTACATGAGCAAAGCCCATGGCATTGACCCTAACATTAGGACAGGCGTCAGGACAATCACAACCGGA : HepCla Segment# : 86 Offset : 1276 1st Codon : 1 I D P N I R T G V R T I T T G S P I T Y S T Y G K F L A D G $\tt ATCGATCCCAATATCAGAACCGGAGTGAGAACCATTACCACAGGCTCCCCCATTACCTATAGCACATACGGAAAGTTTCTGGCTGACGGA$ Segment# : 87 Offset : 1291 1st Codon : 1 S P I T Y S T Y G K F L A D G G C S G G A Y D I I I C D E C AGCCCTATCACATACTCCACCTATGGCAAATTCCTCGCCGATGGCGGATGCTCCGGCGGAGCCTATGACATTATCATTTTGCGATGAGTGT Gene : HepCla Segment# : 88 Offset : 1306 1st Codon : 1 G C S G G A Y D I I I C D E C H S T D A T S I L G I G T V L : HepCla Segment# : 89 Offset : 1321 1st Codon : 1 H S T D A T S I L G I G T V L D Q A E T A G A R L V V L A T CACTCCACCGATGCCACAAGCATTCTGGGAATCGGAACCGTCCTGGATCAGGCTGAGACAGCCGGAGCCAGACTGGTCGTCGCCACA Gene : HepCla Segment# : 90 Offset : 1336 1st Codon : 1 ${\tt GACCAAGCCGAAACCGCTGGCGCTAGGCTCGTGGTCCTGGCTACCGCTACCCGTACCCGGAAGCGTCACCGTCCCCATCCCAATATCGAA}$: HepCla Segment# : 91 Offset : 1351 1st Codon : 1 A T P P G S V T V P H P N I E E V A L S T T G E I P F Y G K GCCACACCCCTGGCTCCGTGACAGTGCCTCACCCTAACATTGAGGAAGTGGCTCTGTCCACCACAGGCGAAATCCCTTTCTATGGCAAA Gene : HepCla Segment# : 92 : 1366 1st Codon : 1 EVALSTTGEIPFYGKAIPLEVIKGGRHLIF GAGGTCGCCCTCAGCACAACCGGAGAGATTCCCTTTTACGGAAAGGCTATCCCTCTGGAAGTGATTAAGGGAGGCAGACACCTCATCTTT : HepCla Segment# : 93 Offset : 1381 1st Codon : 1 A I P L E V I K G G R H L I F C H S K K K C D E L A A K L V Gene : HepCla Segment# : 94 Offset : 1396 1st Codon : 1 C H S K K K C D E L A A K L V A L G I N A V A Y Y R G L D V Gene : HepCla Segment# : 95 Offset : 1411 A L G I N A V A Y Y R G L D V S V I P T S G D V V V V A T D ${\tt GCCCTCGGCATTAACGCTGTGGCTTACTATAGGGGACTGGATGTGTCCGTGATTCCCACAAGCGGAGACGTCGTGGTCGTGGCTACCGATTACCATTACCATTACCATTACCATTACCGATTACCATTACATTACCATTACATTACATTACCATTACATACATTACATTACATTACATACATTACATTACATACATTACATTACATTACATTACATACATTACATTACATTACATACATTACATACATACATACATTACATA$

120/216

Gene : HepCla Segment# : 96 Offset : 1426 lst Codon : 1

S V I P T S G D V V V V A T D A L M T G Y T G D F D S V I D AGCGTCATCCCTACCTCCGGCGATGTGGTCGTCGCCACAGACGCTCTGATGACCGGATACACAGGCGATTTCGATAGCGTCATCGAT

Gene : HepCla Segment# : 97 Offset : 1441 1st Codon : 1

A L M T G Y T G D F D S V I D C N T C V T Q T V D F S L D P GCCCTCATGACAGGCTATACCGGAGACTTTGACTCCGTGATTGACTGTAACACATGCGTCACCCAAACCGTCGACTTTAGCCTCGACCCT

Gene : HepCla Segment# : 98 Offset : 1456 1st Codon : 1

lst Codon: 1
C N T C V T Q T V D F S L D P T F T I E T T T L P Q D A V S
TGCAATACCTGTGTGACACCAGACAGCCTGTGTCC

Gene : HepCla Segment# : 99 Offset : 1471 1st Codon : 1

Gene : HepCla Segment# : 100 Offset : 1486 1st Codon : 1

Gene : HepCla Segment# : 101 Offset : 1501 lst Codon : 1

Y R F V A P G E R P S G M F D S S V L C E C Y D A G C A W Y TACAGATTCGTCGCCCTGGCGAAAGGCCTAGCGGAATGTTTGACTCCAGCGTCCTGTGTGAGTGTTACGATGCCGGATGCGCTTGGTAT

Gene : HepCla Segment# : 102 Offset : 1516 1st Codon : 1

S S V L C E C Y D A G C A W Y E L T P A E T T V R L R A Y M AGCTCCGTGCTCTGCGAATGCTATGACGCTGGGCTTGCTGCTGCTACGACCCGCTGAGACAACCGTCAGGCCTCAGGCTTACATG

Gene : HepCla Segment# : 103 Offset : 1531 1st Codon : 1

ELTPAETTVRLRAYMNTPGLPVCQDHLEFWGGGCTCACCCCTGCCCAAGACCATCTGGAATCTGG

Gene : HepCla Segment# : 104 Offset : 1546 lst Codon : 1

N T P G L P V C Q D H L E F W E G V F T G L T H I D A H F L AACACACCCGGACTGCCTGTGTCAGGGATCACCCTCGAGTTTTCGGAAGGCGTCTTCACAGGCCTCACCCATATCGATGCCCATTTCCTC

Gene : HepCla Segment# : 105 Offset : 1561 1st Codon : 1

1st Codon: 1
E G V F T G L T H I D A H F L S Q T K Q S G E N F P Y L V A
GAGGGAGTGTTTACCGGACTGACACACTTGACGCTCACTTCTGTCCCAGACAAAGCAAAGCGAGAGAATTTCCCTTACCTCGTGGCT

Gene : HepCla Segment# : 106

121/216 Offset : 1576 1st Codon : 1 S Q T K Q S G E N F P Y L V A Y Q A T V C A R A Q A P P P S Gene : HepCla Segment# : 107 Offset : 1591 1st Codon : 1 Y O A T V C A R A Q A P P P S W D Q M W K C L I R L K P T L ${\tt TACCAAGCCACAGTGTGTGCCAGAGCCCAAGCCCCTAGCTGGGACCAAATGTGGAAGTGTCTGATTAGGCTCAAGCCTACCCTC}$: HepCla Segment# : 108 Offset : 1606 1st Codon : 1 W D Q M W K C L I R L K P T L H G P T P L L Y R L G A V O N $\tt TGGGATCAGATGTGGAAATGCCTCATCAGACTGAAACCCACACTGCATGGCCCTACCCCTCTGCTCTACAGACTGGGAGCCGTCCAGAAT$ Gene : HepCla Segment# : 109 Offset : 1621 1st Codon : 1 H G P T P L L Y R L G A V Q N E V T L T H P V T K Y I M T C ${\tt CACGGACCCACACCCCTGTGTATAGGCTCGGCGCTGTGCAAAACGAAGTGACACTGACACACCCTGTGACAAAGTATATCATGACCTGT}$ Gene : HepCla Segment# : 110 Offset : 1636 1st Codon : 1 EVTLTHPVTKYIMTCMSADLEVVTSTWVLV Gene : HepCla Segment# : 111 : 1651 1st Codon : 1 $\begin{smallmatrix} M \end{smallmatrix} \ \, S \ \, A \ \, D \ \, L \ \, E \ \, V \ \, V \ \, T \ \, S \ \, T \ \, W \ \, V \ \, L \ \, V \ \, G \ \, G \ \, V \ \, L \ \, A \ \, A \ \, L \ \, A \ \, Y \ \, C \ \, L \ \, S \ \, T \ \, G$: HepCla Segment# : 112 Offset : 1666 1st Codon : 1 G G V L A A L A A Y C L S T G C V V I V G R I V L S G K P A ${\tt GGCGGAGTGCTCGCCGCTATTGCCTCAGCACACGGCTGTGTGTCATCGTCGGCAGAATCGTCCTGTCCGGCAAACCCGCT}$ Gene : HepCla Segment# : 113 Offset : 1681 1st Codon : 1 C V V I V G R I V L S G K P A I I P D R E V L Y R E F D E M : HepCla Gene Segment# : 114 Offset : 1696 1st Codon : 1 I I P D R E V L Y R E F D E M E E C S Q H L P Y I E Q G M M : HepCla Segment# : 115 : 1711 Offset 1st Codon : 1 E E C S Q H L P Y I E Q G M M L A E Q F K Q K A L G L L Q T

Gene : HepCla Segment# : 116 Offset : 1726 1st Codon : 1

LAEQFKQKALGLLQTASRQAEVIAPAVQTN

GAGGAATGCTCCCAGCATCTGCCTTACATTGAGCAAGGCATGATGCTCGCCGAACAGTTTAAGCAAAAGGCTCTGGGACTGCTCCAGACA

122/216

Gene : HepCla Segment# : 117 Offset : 1741 1st Codon : 1

A S R Q A E V I A P A V Q T N W Q K L E V F W A K H M W N F GCCTCCAGGCAAGCCGAAGCGAAGCTGCAGCAAACTGGCAGAAACTGGAAGTGTTTTGGGCTAAGCATATGTGGAACTTT

Gene : HepCla Segment# : 118 Offset : 1756 1st Codon : 1

Gene : HepCla Segment# : 119 Offset : 1771 1st Codon : 1

I S G I Q Y L A G L S T L P G N P A I A S L M A F T A A V T ATCTCCGGCATTCAGTATCTGGCTGGCCTCAGCACACTGCCTGGCAATCCCGCTATCGCTAGCCTCATGGCTTTCACAGCCGCTGTGACA

Gene : HepCla
Segment# : 120
Offset : 1786
1st Codon : 1

N P A I A S L M A F T A A V T S P L T T S Q T L L F N I L G AACCCTGCCTGATGGCCTTTACCGCTGCCGTCACCTCCCCCTCACCACAAGCCAAACCCTCCTGTTTAACATTCTGGGA

Gene : HepCla Segment# : 121 Offset : 1801 1st Codon : 1

Gene : HepCla Segment# : 122 Offset : 1816 lst Codon : 1

Gene : HepCla Segment# : 123 Offset : 1831 1st Codon : 1

Gene : HepCla Segment# : 124 Offset : 1846 lst Codon : 1

Gene : HepCla Segment# : 125 Offset : 1861 1st Codon : 1

Gene : HepCla Segment# : 126 Offset : 1876 1st Codon : 1

lst Codon: 1

PSTEDLVNLLPAILSPGALVVGVCAAILR
CCCTCCACCGAAGACCTCGTGAATCTGCTCCCCGCTATCCTCAGCCCTGGCGCTCTGGTGGGGAGTGGTCTGCGCTGCCATTCTGAGA

Gene : HepCla

123/216 Segment# : 127 Offset: : 1891 1st Codon : 1 P G A L V V G V V C A A I L R R H V G P G E G A V Q W M N R $\tt CCCGGAGCCCTCGTGGTCGGCGTGTGTGCCGCTATCCTCAGGAGACACGTCGGCCCTGGCGAAGGCGCTGTGCAATGGATGAACAGA$: HepCla Segment# : 128 Offset : 1906 1st Codon : 1 R H V G P G E G A V Q W M N R L I A F A S R G N H V S P T H AGGCATGTGGGACCCGGAGAGGGAGCCGTCCAGTGGATGAATAGGCTCATCGCTTTCGCTAGCAGAGGCAATCACGTCAGCCCTACCCATGene : HepCla Segment# : 129 : 1921 Offset 1st Codon : 1 LIAFASRGNHVSPTHYVPESDAAARVTAIL $\tt CTGATTGCCTTCCAGGGGAAACCATGTGTCCCCCACACACTATGTGCCTGAGTCCGACGCTGCGCTAGGGTCACCGCTATCCTC$: HepCla Segment# : 130 Offset : 1936 1st Codon : 1 Y V P E S D A A A R V T A I L S S L T V T Q L L R R L H Q W TACGTCCCCGAAAGCGATGCCGCTGCCAGAGTGACAGCCATTCTGTCCAGCCTCACCGTCACCCAACTGCTCAGGAGACTGCATCAGTGG Gene : HepCla Segment# : 131 : 1951 Offset 1st Codon : 1 S S L T V T Q L L R R L H Q W I S S E C T T P C S G S W L R Gene : HepCla Segment# : 132 : 1966 Offset 1st Codon : 1 I S S E C T T P C S G S W L R D I W D W I C E V L S D F K T ATCTCCAGCGAATGCACAACCCCTTGCTCCGGCTCCTGGCTCAGGGATATCTGGGACTGTGAGGTCCTGTCCGACTTTAAGACA Gene : HepCla Segment# : 133 : 1981 1st Codon : 1 D I W D W I C E V L S D F K T W L K A K L M P Q L P G I P F ${\tt GACATTGGGATTGCGAAGTGCTCAGCGATTTCAAAACCTGGCTGAAAGCCAAACTGATGCCCCAACTGCCTTTCCCTTT}$: HepCla Segment# : 134 Offset : 1996 1st Codon : 1 W L K A K L M P Q L P G I P F V S C Q R G Y K G V W R G D G Gene : HepCla Segment# : 135 Offset : 2011 1st Codon : 1

V S C Q R G Y K G V W R G D G I M H T R C H C G A E I T G H

Gene : HepCla Segment# : 136 : 2026 Offset

I M H T R C H C G A E I T G H V K N G T M R I V G P R T C R

: HepCla Segment# : 137 Offset : 2041 1st Codon : 1

124/216

Gene : HepCla Segment# : 138 Offset : 2056 1st Codon : 1

N M W S G T F P I N A Y T T G P C T P L P A P N Y T F A L W AACATGTGGTCCGGCACATTCCCTATCAATGCCTATACCACAGGCCCTTGCACACCCCTCCCCGCTCCCAATTACACATTCGCTCTGTGG

Gene : HepCla
Segment# : 139
Offset : 2071
1st Codon : 1

PCTPLPAPNYTFALWRVSAEEYVEIRRVGDCCCCTGTACCCTCTGGAGAGTGTCCGCCGAAGAGTATGTGGAAATCAGAAGGGTCGGCGAT

Gene : HepCla
Segment# : 140
Offset : 2086
1st Codon : 1

R V S A E E Y V E I R R V G D F H Y V T G M T T D N L K C P AGGGTCAGCGCTGAGGAATACGTCGAGATTAGGAGAGTGGGGAGACTTTCACTATGTGACAGGCATGACCACAGACAATCTGAAATGCCCT

Gene : HepCla Segment# : 141 Offset : 2101 1st Codon : 1

F H Y V T G M T T D N L K C P C Q V P S P E F F T E L D G V TTCCATTACGTCACCGGAATGACCACCGATAACCTCAAGTGTCCCTGTCAGGTCCCCCCGGAATTCTTTACCGGAACTGGATGGCGTC

Gene : HepCla Segment# : 142 Offset : 2116 lst Codon : 1

C Q V P S P E F F T E L D G V R L H R F A P P C K P L L R E TGCCAAGTGCCTAGCCCTGAGGCTCTCAGGGAAGTGCATAGGTTTTCACAGAGCTCGACGGAGTGAGACTGCATAGGTTTTGCCCCTCCTGTAAGCCTCTGCTCAGGGAA

Gene : HepCla
Segment# : 143
Offset : 2131
1st Codon : 1

R L H R F A P P C K P L L R E E V S F R V G L H E Y P V G S AGGCTCCACAGATTCGCTCCCCTTGCAAACCCCTCCTGAGAGAGGGAAGTGTCCTTCAGAGTGGGACTGCATGAGTATCCCGTCGGCTCC

Gene : HepCla Segment# : 144 Offset : 2146 1st Codon : 1

E V S F R V G L H E Y P V G S Q L P C E P E P D V A V L T S GAGGTCAGCTTTAGGGTCGGCCTCCACGAATACCCTGTGGGAAGCCCAACTGCCTTGCGAACCCGAACCCGATGTGGCTGTGCTCACCTCC

Gene : HepCla Segment# : 145 Offset : 2161 1st Codon : 1

Gene : HepCla
Segment# : 146
Offset : 2176
1st Codon : 1

Gene : HepCla
Segment# : 147
Offset : 2191
1st Codon : 1

R L A R G S P P S M A S S S A S Q L S A P S L K A T C T A N AGGCTCGCCAGGCTCCCCAGGCTCCCAGCTCCAGCCTCCAGCCACATCCACACCCAAT

125/216

Gene : HepCla Segment# : 148 Offset : 2206 1st Codon : 1

S Q L S A P S L K A T C T A N H D S P D A E L I E A N L L W AGCCAACTGTCCGCCCCTAGCCTCAAGGCTACCTGTAGCGCTAACCATGACTCCCGATGCCGAACTGATTGAGGCTAACCTCCTGTGG

Gene : HepCla
Segment# : 149
Offset : 2221
lst Codon : 1

H D S P D A E L I E A N L L W R Q E M G G N I T R V E S E N CACGATAGCCCTGACGCTCGAGCCCAATCTGCTCTGGAGACAGGAAATGGGAGGCAATATCACAAGGGTCGAGTCCGAGAAT

Gene : HepCla Segment# : 150 Offset : 2236 1st Codon : 1

R Q E M G G N I T R V E S E N K V V I L D S F D P L V A E E AGGCAAGAGAGGGGAAACAATTACCAGAGTGGAAAGCGAAAACAAGTGGTCATCCTCGACTCCTTCGATCCCTCGTGGCTGAGGAA

Gene : HepCla Segment# : 151 Offset : 2251 1st Codon : 1

K V V I L D S F D P L V A E E D E R E I S V P A E I L R K S AAGGTCGTGATTCTGGATAGCTTTGACCCTCTGGTCGCCGAAGAGGATGAGAGAGTTAGCGTCCCCGCTGAGATTCTGAGAAAGTCC

Gene : HepCla Segment# : 152 Offset : 2266 lst Codon : 1

DEREISVPAEILRKSRRFAQALPVWARPDYGACGAAAGGGAAAGGGAAATCCTCAGGAAAAGCAGAAGGTTTGCCCAAGCCCTCCCGTCTGGGCTAGGCCTGACTAT

Gene : HepCla Segment# : 153 Offset : 2281 lst Codon : 1

R R F A Q A L P V W A R P D Y N P P L V E T W K K P D Y E P AGGAGATTCGCTCAGGCTCTGCCTGTGTGGGCCAGACCCGATTACAATCCCCCTCTGGTCGAGACATGGAAAAAGCCTGACTATGAGCCT

Gene : HepCla Segment# : 154 Offset : 2296 1st Codon : 1

N P P L V E T W K K P D Y E P P V V H G C P L P P P R S P P AACCCTCCTCTGGGAAACCCGATTACGAACCCCTTGTGGTCCACGGATGCCCTCTGCCTCCCCCTAGGTCCCCCCCT

Gene : HepCla
Segment# : 155
Offset : 2311
1st Codon : 1

PVVHGCPLPPPRSPPVPPRKKRTVVLTES

Gene : HepCla Segment# : 156 Offset : 2326 1st Codon : 1

Gene : HepCla
Segment# : 157
Offset : 2341
1st Codon : 1

T L S T A L A E L A T K S F G S S S T S G I T G D N T T T S ACCCTCAGCACAGCCCTCGGCAACTGGCTACCAAAAGCTTTGGCTCCAGCTCCAGCATTACCGGAGACAATACCACAACCTCC

Gene : HepCla Segment# : 158 Offset : 2356

126/216 1st Codon : 1 S S S T S G I T G D N T T T S S E P A P S G C P P D S D A E AGCTCCAGCACAAGCGGAATCACAGGCGATAACAACCACAAGCTCCGAGCCTGCCCCTAGCGGATGCCCTCCCGATAGCGATGCCGAA Gene : HepCla Segment# : 159 : 2371 Offset 1st Codon : 1 SEPAPSGCPPDSDAESYSSMPPLEGEPGDP Gene : HepCla Segment# : 160 : 2386 Offset S Y S S M P P L E G E P G D P D L S D G S W S T V S S E A G Gene : HepCla Segment# : 161 Offset : 2401 1st Codon : 1 GACCTCAGCGATGGCTCCTGGTCCACCGTCAGCTCCGAGGCTGGCACAGAGGATGTGGTCTGCTGTAGCATGAGCTATAGCTGGACCGGA Gene : HepCla Segment# : 162 Offset : 2416 1st Codon : 1 T E D V V C C S M S Y S W T G A L V T P C A A E E Q K L P I ${\tt ACCGAAGACGTCGTGTTGCTCCATGTCCTACTCCTGGACAGGCGCTCTGGTCACCCCTTGCGCTGCCGAAGAGCAAAAGCTCCCCATT}$: HepCla Segment# : 163 Offset : 2431 1st Codon : 1 A L V T P C A A E E Q K L P I N A L S N S L L R H H N L V Y GCCCTCGTGACACCCTGTGCCGCTGAGGAACAGAAACTGCCTATCAATGCCCTCAGCAATAGCCTCCTGAGACACCATAACCTCGTGTAT Gene : HepCla Segment# : 164 Offset : 2446 1st Codon : 1 N A L S N S L L R H H N L V Y S T T S R S A C Q R Q K K V T Gene : HepCla Segment# : 165 Offset : 2461 1st Codon : 1 STTSRSACQRQKKVTFDRLQVLDSHYQDVL AGCACAACCTCCAGGTCCGCCTGTCAGAGACAGAAAAAGGTCACCTTTGACAGACTGCAAGTGCTCGACTCCCACTATCAGGATGTGCTC Gene : HepCla Segment# : 166 : 2476 F D R L Q V L D S H Y Q D V L K E V K A A A S K V K A N L L ${\tt TTCGATAGGCTCCAGGTCCTGGATAGCCATTACCAAGACGTCCTGAAAGAGGCTGCAGCCAAGCTGAAAGTGAAAGCCAATCTGCTC}$ Gene : HepCla Segment# : 167 Offset : 2491 K E V K A A A S K V K A N L L S V E E A C S L T P P H S A K ${\tt AAGGAAGTGAAAGCCGCTGCCTCCAAGGTCAAGGCTAACCTCCTGTCCGTGGAAGAGGCTTGCTCCCTGACACCCCCTCACTCCGCCAAA}$: HepCla Gene Segment# : 168 Offset : 2506 1st Codon : 1 $\mathtt{S} \quad \mathtt{V} \quad \mathtt{E} \quad \mathtt{E} \quad \mathtt{A} \quad \mathtt{C} \quad \mathtt{S} \quad \mathtt{L} \quad \mathtt{T} \quad \mathtt{P} \quad \mathtt{P} \quad \mathtt{H} \quad \mathtt{S} \quad \mathtt{A} \quad \mathtt{K} \quad \mathtt{S} \quad \mathtt{K} \quad \mathtt{F} \quad \mathtt{G} \quad \mathtt{Y} \quad \mathtt{G} \quad \mathtt{A} \quad \mathtt{K} \quad \mathtt{D} \quad \mathtt{V} \quad \mathtt{R} \quad \mathtt{C} \quad \mathtt{H} \quad \mathtt{A} \quad \mathtt{R}$

Figure 26 (Cont)

 ${\tt AGCGTCGAGGAAGCCTGTAGCCTCACCCCTCCCCATAGCGCTAAGTCCAAGTTTTGGCTATGGCGCTAAGGATGTGAGATGCCATGCCAGAGATGTCGAGATGTCGAGATGTCGAGATGTGAGATGTCAAGTTTTGGCTATGGCGCTAAGGATGTGAGATGCCATGCCAGAGATGTCGAGATGTCAAGTTTTGGCTATGGCGCTAAGGATGTGAGATGTCAAGTTTTGGCTATGGCGCTAAGGATGTGAGATGCCATGCCAGAGATGTCAAGTTTTGGCTATGGCGCTAAGGATGTGAGATGCCATGCCAGAGATGTCAAGTTTTGGCTATGGCGCTAAGGATGTGAGATGCCATGCCAGAGATGTCAAGTTTTGGCTATGGCGCTAAGGATGTGAGATGCCATGCCAGAGATGTCAAGTTTTGGCTATGGCGCTAAGGATGTTGAGATGCCATGCCAGAGATGTCAAGTTTTGGCTATGGCGCTAAGGATGTTGAGATGCCATGCCAGAGATGTCAAGTTTTGGCTATGGCGCTAAGGATGTTGAGATGCCATGCCAGAGATGTCAAGTTTTGGCTATGGCGCTAAGGATGTTGAGATGTCAAGTTTTGAGAGATGTTAAGTTAAGTTCAAGTTTTGGCTATGGCGATGTTAAGTTGAGATGTCAAGTTTTGAGAGATGTTAAGTAAGTTAAGTTAAGTTAAGTTAAGTTAAGTAAGTTAAGTAAGTTAAGTTAAGTTAAGTTAAGTTAAGTTAAGTAAGTTAAGTTAAGTAAGTTAAGTTAAGTTAAGTTAAGTTAAGTTAAGTTAAGTTAAGTTAAGTTAAGTTAAGTTAAGTTAAGTTAAGTTAAGTTAAGTTAAGTTAAGTAAGTTAAGTTAAGTTAAGTAAGTTAAGTTAAGTTAAGTTAAGTTAAGTAAGTTAAGTTAAGTAAGTTAAGTTAAGTTAAGTAAGT$

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Gene : HepCla Segment# : 169 Offset : 2521 1st Codon : 1

S K F G Y G A K D V R C H A R K A V A H I N S V W K D L L E AGCAAATTCGGATACGGACCCAAAGACGTCAGGTGTCACGCTAGGAAAGCCCTCCGGAAAGACGTCTCGGAAAGACCTCCTGGAA

Gene : HepCla Segment# : 170 Offset : 2536 1st Codon : 1

Gene : HepCla Segment# : 171 Offset : 2551 1st Codon : 1

Gene : HepCla Segment# : 172 Offset : 2566 1st Codon : 1

V F C V Q P E K G G R K P A R L I V F P D L G V R V C E K M GTGTTTTGCGTCCAGCCTGAGAAAGGCGGAAGGAAACCCGCTAGGCTCATCGTCTTCCCTGACCTCGGCGTCAGGGTCTGCGAAAAGATG

Gene : HepCla .
Segment# : 173
Offset : 2581
1st Codon : 1

Gene : HepCla Segment# : 174 Offset : 2596 lst Codon : 1

A L Y D V V S K L P L A V M G S S Y G F Q Y S P G Q R V E F GCCCTCTACGATGTGGTCAGCAACTGCCTCTGGCTGTGATGGGCTCCAGCTATGGCTTTCAGTATAGCCCTGGCCAAAGGGTCGAGTTT

Gene : HepCla Segment# : 175 Offset : 2611 1st Codon : 1

S S Y G F Q Y S P G Q R V E F L V Q A W K S K K T P M G F S AGCTCCTACGGATTCCCCCGGACAGAGAGTGGAATTCCTCGTGCAAGCCTGGAAGTCCAAGAAAACCCCTATGGGATTCTCC

Gene : HepCla Segment# : 176 Offset : 2626 1st Codon : 1

L V Q A W K S K K T P M G F S Y D T R C F D S T V T E S D I CTGGTCCAGGCTTGGAAAAGCAAAAAGACACCCATGGGCTTTAGCTATGACACAAGGTGTTTCGATAGCACAGTGACAGAGTCCGACATT

Gene : HepCla Segment# : 177 Offset : 2641 1st Codon : 1

Gene : HepCla Segment# : 178 Offset : 2656 1st Codon : 1

R T E E A I Y Q C C D L D P Q A R V A I K S L T E R L Y V G
AGGACAGAGGAAGCCATTACCAATGCTGTGACCTCGACCCTCAGGCTAGGGTCGCCATTAAGTCCCTGACAGAGAGACTGTATGTGGGA

Gene : HepCla Segment# : 179

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Offset : 2671 1st Codon : 1

A R V A I K S L T E R L Y V G G P L T N S R G E N C G Y R R GCCAGAGGGCTATCAAAAGCCTCACCGAAAGGCTCTACGTCGGCGGACCCCTCACCAATAGCAGAGGGCGAAAACTGTGGCTATAGGAGA

Gene : HepCla Segment# : 180 Offset : 2686 1st Codon : 1

G P L T N S R G E N C G Y R R C R A S G V L T T S C G N T L $\tt GGCCCTCTGACAAACTCCAGGGGGAGAATTGCGGATACAGAAGGTGTAGGGGCTAGCGGAGTGCTCACCACAAGCTGTGGCAATACCCTC$

Gene : HepCla
Segment# : 181
Offset : 2701
1st Codon : 1

C R A S G V L T T S C G N T L T C Y I K A R A A C R A A G L TGCAGAGCCTCCGGCGTCCTGCCGACACCTCCTGCGAAACACTGACATGCTATATCAAAGCCAGAGCCGCTTGCAGAGCCGCTGGCCTC

Gene : HepCla Segment# : 182 Offset : 2716 1st Codon : 1

T C Y I K A R A A C R A A G L Q D C T M L V C G D D L V V I ACCTGTTACATTAAGGCTAGGGCTGCCTGTAGGGCTGCCGGACTGCAGACTGTACCATGCTGGTCTGGGAGACGATCTGGTCGTGATT

Gene : HepCla Segment# : 183 Offset : 2731 lst Codon : 1

Q D C T M L V C G D D L V V I C E S A G V Q E D A A S L R A CAGGATTGCACAATGCTCGTGTGTGACCTCGTGGTCATCTGTGAGTCCGCCGGAGTGCAAGAGGATGCCGCTAGCCTCAGGGCT

Gene : HepCla Segment# : 184 Offset : 2746 1st Codon : 1

C E S A G V Q E D A A S L R A F T E A M T R Y S A P P G D P TGCGAAAGCGCTGGCGTCCAGGAAGACGCTGCCTCCCGGAGACCCTTTACCGAAGCCATGACCAGATACTCCGCCCCTCCCGGAGACCCT

Gene : HepCla
Segment# : 185
Offset : 2761
1st Codon : 1

F T E A M T R Y S A P P G D P P Q P E Y D L E L I T S C S S TTCACAGAGGCTATGACAAGGTATAGCGCTCCCCTGGCGATCCCCCTCAGCCTGAGCTATGACCTCACAAGCTGTAGCTCC

Gene : HepCla Segment# : 186 Offset : 2776 1st Codon : 1

PQPEYDLELITSCSSNVSVAHDGAGKRVYYCCCCCAACCCGAATACGATCTGGAACTGATTACCTCCTGCTCCAGCAATGTGTCCGTGGCTCACGATGGCGCTGGCAAAAGGGTCTACTAT

Gene : HepCla
Segment# : 187
Offset : 2791
1st Codon : 1

Gene : HepCla Segment# : 188 Offset : 2806 1st Codon : 1

1st Codon: 1
L T R D P T T P L A R A A W E T A R H T P V N S W L G N I I
CTGACAAGGGATCCCACAACCCCTCTGGCTAGGGCTGCCTGGGAGACACCCAGACACACCCCGTCAACTCCTGGCTCGGCAATATCATT

Gene : HepCla Segment# : 189 Offset : 2821 1st Codon : 1

T A R H T P V N S W L G N I I M F A P T L W A R M I L M T H

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Gene : HepCla Segment# : 190 Offset : 2836 1st Codon : 1

M F A P T L W A R M I L M T H F F S V L I A R D Q L E Q A L ATGTTTGCCCTACCCTCTGGGCTAGGATGATCCTCATGACACACTTTTTCTCCGTGCTCATCGCTAGGGATCAGCTCGAGCAAGCCCTC

Gene : HepCla Segment# : 191 Offset : 2851 1st Codon : 1

Gene : HepCla Segment# : 192 Offset : 2866 1st Codon : 1

D C E I Y G A C Y S I E P L D L P P I I Q R L H G L S A F S GACTGTGAGATTTACGGAGCCTGTTACTCCATCGACCCCCCTATCATTCAGAGACTGCATGGCCTCAGCGCTTTCTCC

Gene : HepCla Segment# : 193 Offset : 2881 1st Codon : 1

L P P I I Q R L H G L S A F S L H S Y S P G E I N R V A A C CTGCCTCCCATTATCCAAAGGCTCCACGGACTGTCCGCCTTTAGCCTCCACTCCTACTCCCCCGGAGAGATTAACAGAGTGGCTGCCTGT

Gene : HepCla Segment# : 194 Offset : 2896 lst Codon : 1

L H S Y S P G E I N R V A A C L R K L G V P P L R A W R H R CTGCATAGCTATAGCCCTGGCGAAATCAATAGGGTCGCCGCTTGCCTCAGGAAACTGGGAGTGCCTCCCCTCAGGGCTTGGAGACACAGA

Gene : HepCla Segment# : 195 Offset : 2911 1st Codon : 1

LRKLGVPPLRAWRHRARSVRARLLARGGRAGGCAGAGGCGGAAGGCCTGGGAAAAGCTCCGCCTCTGAGAGCCTGGAGGCCTAGGGCTAGGCTCCGTGAGAGCCAGACTGCTCGCCAGAGGCGGAAGGGCT

Gene : HepCla Segment# : 196 Offset : 2926 1st Codon : 1

A R S V R A R L L A R G G R A A I C G K Y L F N W A V R T K GCCAGAAGCGTCAGGGCTCTGGCTAGGGGAGCCAGAGCCAAATACCTCTTCAATTGGGCTGTGAGAACCAAA

Gene : HepCla Segment# : 197 Offset : 2941 1st Codon : 1

A I C G K Y L F N W A V R T K L K L T P I A A A G R L D L S GCCATTGCGGAAAGTATCTGTTTAACTGGGCCGTCAGGACAAAGCTCAAGCTCACCCCTATCGCTGCCGCTGGCAGACTGGATCTGTCC

Gene : HepCla Segment# : 198 Offset : 2956 lst Codon : 1

Gene : HepCla Segment# : 199 Offset : 2971 1st Codon : 1

G W F T A G Y S G G D I Y H S V S H A R P R W F W F C L L L GGCTGGTTCACAGCCGGATACTCCGGCGGAGACATTTACCATAGCGTCAGCCATGCCAGACCCAGATGGTTTTGGTTTTGCCTCCTGCTC

Gene : HepCla

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Segment# : 200 Offset : 2986 1st Codon : 1

Gene : HepCla Segment# : 201 Offset : 3001 1st Codon : 1

L A A G V G I Y L L P N R A A CTGGCTGCCGGAGTGGGAATCTATCTGCTCCCCAATAGGGCTGCC

Segments in scrambled order:

HepCla #77

V I P V R R R G D S R G S L L S P R P I S Y L K G S S G G P GTGATTCCCGTCAGGAGAAGGGTCCAGGGGAAGCCTCTGTCCCCCAGACCCATTAGCTATCTGAAAGGCTCCAGCGGAGGCCCT

HepCla #68

A R R G R E I L L G P A D G M V S K G W R L L A P I T A Y A GCCAGAAGGGGAAGGGAAAGGCTCCTGGCTCCCATTACCGCTTACCGCT

HepCla #143

HepCla #66

V V F S Q M E T K L I T W G A D T A A C G D I I N G L P V S GTGGTCTTCTCCCAGATGGAGACAAAGCTCATCACATGGGGAGCCGATACCGCTGCCTGTGGCGATATCATTAACGGACTGCCTGTGTCC

HepCla #79

L L C P A G H A V G I F R A A V C T R G V A K A V D F I P V CTGCTCTGCCCTGCCGGACACGCTGTGGGAATCTTTAGGCTGCCGTCTGCACAAGGGGAGTGGCTAAGGCTGTGGATTTCATTCCCGTC

HepCla #113

C V V I V G R I V L S G K P A I I P D R E V L Y R E F D E M TGCGTCGTGATTGTGGGAAGGTTCGATCGGAAAGCCTGCCATTATCCCTGACAGAGAGGTCCTGTATAGGGAATTCGATGAGATG

HepCla #139

PCTPLPAPNYTFALWRVSAEEYVEIRRVGDCCCTGTACCTCTGCACCTCTGCACGAGAGTCTCCCCCGAAGAGTATGTGGAAATCAGAAGGGTCGCCGAT

HepC1a #174

A L Y D V V S K L P L A V M G S S Y G F Q Y S P G Q R V E F GCCCTCTACGATGTGGTCAGCAAACTGCCTCTGGCTGTGATGGGCTCCAGCTATGGCTTTCAGTATAGCCCTGGCCAAAGGGTCGAGTTT

HepCla #57

I S W C L W W L Q Y F L T R V E A Q L H V W V P P L N V R G ATCTCCTGGTGTCTGTGGTGGCTCCAGTATTTCCTCACCAGAGTGGAAGCCCAACTGCATGTGTGGGTGCCTCCCCTCAACGTCAGGGGA

HepCla #51

ENLVILNAASLAGTHGLVSFLVFFCFAWYL

HepC1a #193

L P P I I Q R L H G L S A F S L H S Y S P G E I N R V A A C CTGCCTCCCATTATCCAAAGGCTCCACGGACTGTCCGCCTTTAGCCTCCACTCCTACTCCCCCGGAGAGATTAACAGAGTGGCTGCTTGT

HepCla #154

N P P L V E T W K K P D Y E P P V V H G C P L P P P R S P P AACCCTCCCTCTGGAAAACCCGATTACGAACCCCCTGTGGTCCACGGATGCCTCTGCCTCCCCCTAGGTCCCCCCCT

HepCla #48

HepCla #37

f LN N T R P P L G N W F G C T W M N S T G F T K V C G A P P CTGAATAACACAAGGCCTCCCCTCGGCAATTGGTTTGGCTGTACCTGGATGAATAGCACAGGCTTTACCAAAGTGTGTGGCGCTCCCCCT

HepC1a #185

F T E A M T R Y S A P P G D P P Q P E Y D L E L I T S C S S

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HepCla #54

HepCla #70

Q T R G L L G C I I T S L T G R D K N Q V E G E V Q I V S CAGCAAACCAGAGGCCTCCTGGGATGCATTATCACAAGCCTCACCGGAAGGGATAAGAATCAGGTCGAGGGAGAGGTCCAGATTGTGTCC

HepCla #82

HepCla #104

N T P G L P V C Q D H L E F W E G V F T G L T H I D A H F L AACACCCCGGACTGCCTGTGTCAGGATCACCTCGAGTTTTGGGAAGGCGTCTTCACAGGCCTCACCCATATCGATGCCCATTTCCTC

HepCla #26

V L L F A G V D A E T H V T G G N A G R T T S G L V S L L GTGCTCCTGCTCTCGCTGGCGCTGAGACACCTCACCGGAGGCAATGCCGGAAGGACAACCTCCGGCCTCGTGTCCCTGCTC

HepCla #110

HepCla #56

V G L M A L T L S P Y Y K R Y I S W C L W W L Q Y F L T R V GTGGGACTGATGGCCCTCACCCTCAGCCCTTACTATAAGAGATACATTAGCTGGTGCCTCTGGTGGCTGCAATACTTTCTGACAAGGGTC

HepCla #197

A I C G K Y L F N W A V R T K L K L T P I A A A G R L D L S GCCATTGCGGAAAGTATCTGTTTAACTGGGCCGTCAGGACAAAGCTCAAGCTCACCCCTATCGCTGCCGCTGGCAGACTGGATCTGTCC

HepCla #25

I À Y F S M V G N W A K V L V V L L L F A G V D A E T H V T ATCGCTTACTTTAGCATGGTGGGAAACCCATGTGACA

HepCla #147

HepCla #52

G L V S F L V F F C F A W Y L K G R W V P G A V Y A L Y G M GGCCTCGTGTCCTCGTGTTTTCTGTTTCGCTTGGTATCTGAAAGGCAGATGGGTCCCCGGAGCCGTCTACGCTCTGTATGGCATG

HepCla #145

Q L P C E P E P D V A V L T S M L T D P S H I T A E A A G R CAGCTCCCCTGTGAGCCTGACGTCCTGACGAGCCTGACAGCCCTAGCCATATCACAGCCGAAGCCGCTGGCAGA

HepCla #171

DSVTPIDTTIMAKNEVFCVQPEKGGRKPARGGCTGCCAGA

HepCla #84

Y A A Q G Y K V L V L N P S V A A T L G F G A Y M S K A H G TACGCTGCCCAAGGCTATAAGGTCCTGAATCCCTCCGTGGCTGCCACACTGGGATCCGAGCCTATATGTCCAAGGCTCACGGA

HepCla #14

HepCla #175

S S Y G F Q Y S P G Q R V E F L V Q A W K S K K T P M G F S AGCTCCTACGGATTCCCCCGGACAGAGAGTGGAATTCCTCGTGCAAGCCTGGAAGTCCAAGAAAAACCCCTATGGGATTCTCC

HepCla #67

HepCla #148

S Q L S A P S L K A T C T A N H D S P D A E L I E A N L L W AGCCAACTGTCCGCCCTAGCCTCAAGGCTACCTGTTGCGCTAACCATGACTCCCGATGCCGAACTGATTGAGGCTAACCTCCTGTGG

132/216

HepCla #120

HepCla #176

L V Q A W K S K K T P M G F S Y D T R C F D S T V T E S D I CTGGTCCAGGCTTGGAAAAGCAAAAAGACACCCATGGGCTTTAGCTATGACACAAGGTGTTTCGATAGCACAGTGACAGAGTCCGACATT

HepCla #152

D E R E I S V P A E I L R K S R R F A Q A L P V W A R P D Y GACGAAAGGGAAATCTCCGTGCCGAAATCCTCAGGAAAAGCAGAAGGTTTGCCCAAGCCCTCCCGGTCTGGGCTAGGCCTGACTAT

HepCla #190

M F A P T L W A R M I L M T H F F S V L I A R D Q L E Q A L ATGTTTGCCCTACCCTCTGGGCTAGGATGATCCTCATGACACACTTTTTCTCCGTGCTCATCGCTAGGGATCAGCTCGAGCAAGCCCTC

HepCla #96

S V I P T S G D V V V V A T D A L M T G Y T G D F D S V I D AGCGTCATCCCTACCTCCGGCGATGTGGTCGTCGTCGCCACAGACGCTCTGATGACCGGATACACAGGCGATTTCGATAGCGTCATCGAT

HepCla #94

C H S K K K C D E L A A K L V A L G I N A V A Y Y R G L D V TGCCATAGCAAAAAGAAATGCGATGAGCTCGCGCTAAGCTCGTGGCTCTGGGAATCAATGCCGTCGCCTATTACAGAGGCCTCGACGTC

HepCla #46

HepCla #53

K G R W V P G A V Y A L Y G M W P L L L L L A L P Q R A Y AAGGGAAGGTGGGTGCCTGGTGTGTGTGTCCTCTGGAATGTGGCCCTCTTGCTCCTGCTCTCTGGTTTGCCTCAGAGAGCCTAT

HepCla #87

S P I T Y S T Y G K F L A D G G C S G G A Y D I I I C D E C AGCCCTATCACATACTCCACCTATGGCAAATTCĆTCGCCGATGGCGGATGCTCCGGCGGAGCCTATGACATTATCATTTGCGATGAGTGT

HepCla #196

HepCla #170

K[®]AVAHINSVWKDLLEDSVTPIDTTIMAKNE AAGGCTGTGGCTCACATTAACTCCGTGTGGAAGGATCTGCTCGAGGATAGCGTCACCCCTATCGATACCACAATCATGGCCAAAAACGAA

HenCla #35

F T P S P V V V G T T D R S G A P T Y S W G A N D T D V F V
TTCACACCCTCCCCGTCGTCGTCGCCACAACCCGATAGCTCCTCGCGCGCTCCTCCGTC

HepCla #16

PGCVPCVREGNASRCWVAMTPTVATRDGKLCCCGGATGCGTCCCTGTGTGAGAGAGGGAAACGCTAGCAGATGCTGGGTGGCTATGACACCCCACAGTGGCTACCAGAGACGGAAACGCTC

HenCla #183

Q D C T M L V C G D D L V V I C E S A G V Q E D A A S L R A CAGGATTGCACAATGCTCGTGTGGCGATGACCTCGTGGTCATCTGTGAGTCCGCCGGAGTGCAAGAGGATGCCGCTAGCCTCAGGGCT

HepCla #125

HepCla #177

HepCla #103

ELTPAETTVRLRAYMNTPGLPVCQDHLEFW GAGCTCACCCCTGCCGAAACCACAGTGAGACTGAGAGCCTATATGAATACCCCTGGCCTCCCCGTCTGCCAAGACCATCTGGAATTCTGG

HepCla #186

P Q P E Y D L E L I T S C S S N V S V A H D G A G K R V Y Y CCCCAACCCGAATACGATCTGGAACTGATTACCTCCTGCTCCAGCAATGTGTCCGTGGCTCACGATGGCGCTGGCAAAAGGGTCTACTAT

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HepCla #9

LGKVIDTLTCGFADLMGYIPLVGAPLGGAA

A I P L E V I K G G R H L I F C H S K K K C D E L A A K L V ${\tt GCCATTCCCTCGAGGTCATCAAAGGCGGAAGGCATCTGATTTTCTGTCACTCCAAGAAAAAGTGTGACGAACTGGCTGCCAAACTGGTC}$

G G V L A A L A A Y C L S T G C V V I V G R I V L S G K P A ${\tt GGCGGAGTGCTCGCCGCTATTGCCTCAGCACAGGCTGTGTGTCATCGTCGGCAGAATCGTCCTGTCCGGCAAACCCGCT}$

HepC1a #184

C E S A G V Q E D A A S L R A F T E A M T R Y S A P P G D P TGCGAAAGCGCTGGCGTCCAGGAAGACGCTGCCTCCCTGAGAGCCTTTACCGAAGCCATGACCAGATACTCCGCCCCTCCCGGAGACCCT

G W F T A G Y S G G D I Y H S V S H A R P R W F W F C L L L GGCTGGTTCACAGCCGGATACTCCGGCGGAGACATTTACCATAGCGTCAGCCATGCCAGACCCAGATGGTTTTGGTTTTGCCTCCTGCTC

HepCla #158

S S S T S G I T G D N T T T S S E P A P S G C P P D S D A E AGCTCCAGCACAAGCGGAATCACAGGCGATAACACAACCACAAGCTCCGAGCCTGCCCCTAGCGGATGCCCTCCCGATAGCGATGCCGAA

R T Q R R G R T G R G K P G I Y R F V A P G E R P S G M F D

HepCla #43

V R M Y V G G V E H R L E A A C N W T R G E R C D L E D R D GTGAGAATGTATGTGGGAGGCGTCGAGCATAGGCTCGAGGCTGCCTGTAACTGGACCAGAGGCGAAAGGTGTGACCTCGAGGATAGGGAT

EAQLHVWVPPLNVRGGRDAVILLMCVVHPT

LGVRATRKTSERSQPRGRRQPIPKARRPEG $\tt CTGGGAGTGAGAGCCACAAGGAAAACCTCCGAGAGAAGCCAAACCCAGAGGCAGAAGGCAGAAGCCATTCCCAAAGCCAGAAGGCCTGAGGGA$

N V S V A H D G A G K R V Y Y L T R D P T T P L A R A A W E AACGTCAGCGTCGCCCATGACGGAGCCGGAAAGAGAGTGTATTACCTCACCAGAGACCCCTACCACACCCCTCGCCAGAGCCGCTTGGGAA

S E P A P S G C P P D S D A E S Y S S M P P L E G E P G D P AGCGAACCCGCTCCCTCCGGCTGTCCCCCTGACTCCGACGCTGAGTCCTACTCCAGCATGCCCCTCTGGAAGGCGAACCCGGAGACCCT

HepCla #63

I G G H Y V Q M A I I K L G A L T G T Y V Y N H L T P L R D ATCGGAGGCCATTACGTCCAGATGGCCATTATCAAACTGGGAGCCCTCACCGGAACCTATGTGTATAACCATCTGACACCCCTCAGGGAT

HepCla #126

P S T E D L V N L L P A I L S P G A L V V G V V C A A I L R $\tt CCCTCCACCGAAGACCTCGTGAATCTGCTCCCGCTATCCTCAGCCCTGGCGCTCTGGTGGGAGTGGTCTGCGCTGCCATTCTGAGA$

HepCla #24

I L D M I A G A H W G V L A G I A Y F S M V G N W A K V L V

EGCGWAGWLLSPRGSRPSWGPTDPRRRS_{RN} GAGGGATGCGGATGGCTGGCTGCTCAGCCCTAGGGGAAGCAGACCCTCCTGGGGACCCACAGACCCTAGGAGAAGGTCCAGGAAT

HepCla #21 WTTQGCNCSIYPGHITGHRMAWDMMMNWSP $\tt TGGACAACCCAAGGCTGTAACTGTAGCATTTACCCTGGCCATATCACAGGCCATAGGATGGTGGACATGATGATGAACTGGAGCCCT$

W V A M T P T V A T R D G K L P A T Q L R R H I D L L V G S

HepCla #42

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R L W H Y P C T I N Y T I F K V R M Y V G G V E H R L E A A

V F C V Q P E K G G R K P A R L I V F P D L G V R V C E K M $\tt GTGTTTTGCGTCCAGCCTGAGAAAGGCGGAAGGAAACCCGCTAGGCTCATCGTCTTCCCTGACCTCGGCGTCAGGGTCTGCGAAAAGATG$

HepCla #10 M G Y I P L V G A P L G G A A R A L A H G V R V L E D G V N $\tt ATGGGATACATTCCCCTCGTGGGAGCCCCTCTGGGAGGCGCTGCCAGAGCCCTCGCCCATGGCGTCAGGGTCCTGGAAGACGGAGTGAAT$

G G N A G R T T S G L V S L L T P G A K Q N I Q L I N T N G GGCGGAAACGCTGGCAGAACCACAAGCGGACTGGTCAGCCTCCTGACACCGGAGCCAAACAGAATATCCAACTGATTAACACAAACGGA

HepCla #13

LALLSCLTVPASAYQVRNSTGLYHVTNDCP $\tt CTGGCTCTGCTCAGCTGTCTGACAGTGCCTGCCTCCGCCTATCAGGTCAGGAATAGCACAGGCCTCTACCATGTGACAAACGATTGCCCT$

G R D K N Q V E G E V Q I V S T A A Q T F L A T C I N G V C GGCAGAGACAAAAACCAAGTGGAAGGCGAAGTGCAAATCGTCAGCACAGCCGCTCAGACATTCCTCGCCACATGCATTAACGGAGTGTGT

P A T Q L R R H I D L L V G S A T L C S A L Y V G D L C G S $\tt CCCGCTACCCAACTGAGAAGGCATATCGATCTGCTCGTGGGAAGCGCTACCCTCTGCTCCGCCCTCTACGTCGGCGATCTGTGTGGCTCC$

H A P T G S G K S T K V P A A Y A A Q G Y K V L V L N P S V CACGCTCCCACAGGCTCCGGCAAAAGCACAAAGGTCCCCGCTGCCTATGCCGCTCAGGGATACAAAGTGCTCGTGCTCAACCCTAGCGTC

R T W A Q P G Y P W P L Y G N E G C G W A G W L L S P R G S

T E D V V C C S M S Y S W T G A L V T P C A A E E Q K L P I ${\tt ACCGAAGACGTCGTGTTGCTCCATGTCCTACTCCTGGACAGGCGCTCTGGTCACCCCTTGCGCTGCCGAAGAGCAAAAGCTCCCCATT}$

ALDTEVAASCGGVVLVGLMALTLSPYYKRY GCCCTCGACACAGAGGTCGCCGCTAGCTGTGGCGGAGTGGTCCTGGTCGGCCTCATGGCTCTGACACTGTCCCCCTATTACAAAAGGTAT

HepCla #38

W M N S T G F T K V C G A P P C V I G G A G N N T L H C P T

S V E E A C S L T P P H S A K S K F G Y G A K D V R C H A R AGCGTCGAGGAAGCCTGTAGCCTCACCCCTCCCCATAGCGCTAAGTCCAAGTTTTGGCTATGGCGCTAAGGATGTGAGATGCCATGCCAGA

HepCla #119

I S G I Q Y L A G L S T L P G N P A I A S L M A F T A A V T

Q I V G G V Y L L P R R G P R L G V R A T R K T S E R S Q P ${\tt CAGATTGTGGGAGGCGTCTACCTCCTGCCTAGGAGAGGCCCTAGGCTCGGCGTCAGGGCTACCAGAAGACAAGCGAAAGGTCCCAGCCT}$

HepCla #194

LHSYSPGEINRVAACLRKLGVPPLRAWRHR $\tt CTGCATAGCCTTGGCGAAATCAATAGGGTCGCCGCTTGCCTCAGGAAACTGGGAGTGCCTCCCCTCAGGGCTTGGAGACACAGA$

TARHTPVNSWLGNIIMFAPTLWARMILMTH

ENLETTMRSPVFTDNSSPPAVPQSFQVAHL GAGAATCTGGAAACCACAATGAGAAGCCCTGTGTTTACCGATAACTCCAGCCCTCCCGCTGTGCCTCAGTCCTTCCAAGTGGCTCACCTC

HepCla #91

A T P P G S V T V P H P N I E E V A L S T T G E I P F Y G K

135/216

 ${\tt GCCACACCCCTGGCTCACCGTGACATTGACCTTAACATTGAGGAAGTGGCTCTGTCCACCACAGGCGAAATCCCTTTCTATGGCAAA}$

HepCla #60

LVFDITKLLLAVFGPLWILQASLLKVPYFV $\tt CTGGTCTTCGATATCACAAAGCTCCTGCTCGCCGTCTTCGGACCCCTCTGGATTCTGCAAGCCTCCCTGCTCAAGGTCCCCTATTTCGTC$

T A A L V M A Q L L R I P Q A I L D M I A G A H W G V L A G ACCGCTGCCTCGTGATGGCCCAACTGCTCAGGATTCCCCAAGCCATTCTGGATATGATTGCCGGAGCCCATTGGGGAGTGCTCGCCGGA

HepCla #98 C N T C V T Q T V D F S L D P T F T I E T T L P Q D A V S TGCAATACCTGTGTGACACAGACAGTGGATTTCTCCCTGGATCCCACATTCACAATCGAAACCACAACCCTCCCCCAAGACGCTGTGTCC

HGPTPLLYRLGAVQNEVTLTHPVTKYIMTC CACGGACCCACACCCCTCTGTATAGGCTCGGCGCTGTGCAAAACGAAGTGACACACCCTGTGACAAAGTATATCATGACCTGT

A R V A I K S L T E R L Y V G G P L T N S R G E N C G Y R R ${\tt GCCAGAGTGGCTATCAAAAGCCTCACCGAAAGGCTCTACGTCGGCGGACCCCTCACCAATAGCAGAGGCGAAAACTGTGGCTATAGGAGA}$

HepCla #39

C V I G G A G N N T L H C P T D C F R K H P E A T Y S R C G

T C G S S D L Y L V T R H A D V I P V R R G D S R G S L L

N M W S G T F P I N A Y T T G P C T P L P A P N Y T F A L W ${\tt AACATGTGGTCCGGCACATTCCCTATCAATGCCTATACCACAGGCCCTTGCACACCCCTCCCGGCTCCCAATTACACATTCGCTCTGTGG}$

H S T D A T S I L G I G T V L D Q A E T A G A R L V V L A T CACTCCACCGATGCCACAAGCATTCTGGGAATCGGAACCGTCCTGGATCAGGCTGAGACAGCCGGAGCCAGACTGGTCGTGCTCGCCACA

YVPESDAAARVTAILSSLTVTQLLRRLHQW TACGTCCCCGAAAGCGATGCCGCTGCCAGAGTGACAGCCATTCTGTCCAGCCTCACCGTCACCCAACTGCTCAGGAGACTGCATCAGTGG

R P S W G P T D P R R R S R N L G K V I D T L T C G F A D L AGGCCTAGCTGGGGCCCTACCGATCCCAGAAGGAAGCAGAAACCTCGGCAAAGTGATTGACACACTGACATGCGGATTCGCTGACCTC

HepCla #33

G P .D Q R P Y C W H Y P P K P C G I V P A K S V C G P V Y C

E E C S Q H L P Y I E Q G M M L A E Q F K Q K A L G L L Q T GAGGAATGCTCCCAGCATCTGCCTTACATTGAGCAAGGCATGATGCTCGCCGAACAGTTTAAGCAAAAGGCTCTGGGACTGCTCCAGACA

HepCla #107

Y Q A T V C A R A Q A P P P S W D Q M W K C L I R L K P T L ${\tt TACCAAGCCACAGTGTGTGCCAGAGCCCAAGCCCTTCCCCCTAGCTGGGACCAAATGTGGAAGTGTCTGATTAGGCTCAAGCCTACCCTC}$

C G I V P A K S V C G P V Y C F T P S P V V V G T T D R S G

S S L T V T Q L L R R L H Q W I S S E C T T P C S G S W L R

HepCla #161

D L S D G S W S T V S S E A G T E D V V C C S M S Y S W T G GACCTCAGCGATGGCTCCTGGTCCACCGTCAGCTCCGAGGCTGGCACAGAGGATGTGGTCTGCTGTAGCATGAGCTATAGCTGGACCGGA

W D Q M W K C L I R L K P T L H G P T P L L Y R L G A V Q N TGGGATCAGATGTGGAAATGCCTCATCAGACTGAAACCCACACTGCATGGCCCTACCCCTCTGCTCTACAGACTGGGAGCCGTCCAGAAT

136/216

HepCla #116

L A E Q F K Q K A L G L L Q T A S R Q A E V I A P A V Q T N CTGGCTGAGCAATTCAAACAGAAAGCCCTCGGCCTCCTGCAAACCGCTAGCAGACAGCTGAGGTCATCGCTCCCGCTGTGCAAACCAAT

HepCla #118

W Q K L E V F W A K H M W N F I S G I Q Y L A G L S T L P G TGGCAAAAGCTCGAGGTCTTCTGGGCCAAACACATGTGGAATTTCATTAGCGGAATCCAATACCTCGCCGGACTGTCCACCCTCCCCGGA

HepCla #129

HepCla #19

A T L C S A L Y V G D L C G S V F L V G Q L F T F S P R R H GCCACACTGTGTGAGGGTCTTCTCTCGGGAAGGCAT

HepCla #102

S S V L C E C Y D A G C A W Y E L T P A E T T V R L R A Y M AGCTCCGTGCTGCGAATGCTATGACGCTGGCTGTGCCTGGTACGACTGACACCCGCTGAGACAACCGTCAGGCTCAGGCTTACATG

HepCla #122

HepCla #29

S W H I N S T A L N C N E S L N T G W L A G L F Y Q H K F N AGCTGGCACATTAACTCCACCGCTCTGAATTGCAATGCGCTGGATGCCTGGATGCCTCGCCGGACTGTTTTACCAACACAAATTCAAT

HepCla #164

HepCla #1

A A M S T N P K P Q R K T K R N T N R R P Q D V K F P G G G GCCGCTATGTCCACCAATCCCAAACCCCAAAGGAAAACCAAAAGGAATACCAATAGGAGACCCCAAAGCGTCAAGTTTCCCGGAGGCGGA

HepCla #106

HepCla #36

A P T Y S W G A N D T D V F V L N N T R P P L G N W F G C T GCCCTACCTATAGCTGGGGCGCTAACGATACCGATGCTTTGTGCTCAACAATACCAGACCCCCTCTGGGAAACTGGTTCGGATGCACA

HepCla #156

f V P P R K K R T V V L T E S T L S T A L A E L A T K S F G GTGCCTCCCCTAGGAAAAGGAGAACCGTCGTGCTCACCGAAAGCACCTGTCCACCGCTCTGGCTGAGCTCGCCACAAAGTCCTTCGGA

HepC1a #165

S T T S R S A C Q R Q K K V T F D R L Q V L D S H Y Q D V L AGCACAACCTCCAGGTCCGCCTGTCAGAGACAGAAAAAGGTCACCTTTGACAGACTGCAAGTGCTCGACTCCCACTATCAGGATGTGCTC

HepCla #90

HepCla #141

F H Y V T G M T T D N L K C P C Q V P S P E F T E L D G V TTCCATTACGTCACCGGAATGACAACCGATAACCTCAAGTGTCCCTGTCAGGTCCCCTCCCCCGAATTCTTTACCGAACTGGATGGCGTC

HepC1a #198

HepCla #117

A S R Q A E V I A P A V Q T N W Q K L E V F W A K H M W N F GCCTCCAGGCAAGCCGAAGCGAAGCGAAGCTGTTTTGGGCTAAGCATATGTGGAACTTT

HepC1a #181

C R A S G V L T T S C G N T L T C Y I K A R A A C R A A G L TGCAGAGCCTCCGGCGTCCTGACAACCTCCTGCGGAAACACTGACATGCTATATCAAAGCCAGAGCCGCTTGCAGAGCCGCTGGCCTC

137/216

HepCla #166

F D R L Q V L D S H Y Q D V L K E V K A A A S K V K A N L L TTCGATAGGCTCCAGGTCCTGGATAGCCATTACCAAGACGTCCTGAAAGAGGCTCAAGGCTGCCGCTAGCAAAGTGAAAGCCAATCTGCTC

HepCla #180

G P L T N S R G E N C G Y R R C R A S G V L T T S C G N T L GGCCCTCTGACAAACTCCAGAGGAGAATTGCGGATACAGAAGGTGTAGGGCTAGCGGAGTGCTCACCACAAGCTGTGGCAATACCCTC

HepCla #136

I M H T R C H C G A E I T G H V K N G T M R I V G P R T C R ATCATGCACACAAGGTGTCACTGTGGCGCTGAGATTACCGGACACGTCAAGAATGGCACAATGAGAATCGTCGGCCCTAGGACATGCAGA

HepCla #144

E V S F R V G L H E Y P V G S Q L P C E P E P D V A V L T S GAGGTCAGCTTTAGGGTCGGCCTCCACGAATACCCTGTGGGAAGCCAACTGCCTTGCGAACCCGAACCGATGTGGCTGTGCTCACCTCC

HepCla #167

K E V K A A A S K V K A N L L S V E E A C S L T P P H S A K AAGGAAGTGAAAGCCGCTGCCTCAAGGTCAAGGCTAACCTCCTGTCCGTGGAAGAGGCTTGCTCCCTGACACCCCCTCACTCCGCCAAA

HepCla #59

G R D A V I L L M C V V H P T L V F D I T K L L A V F G P GGCAGAGACGCTGTGTTCTGCTCATGTGTGTGTGTCCTACCCTACCCTGTGTTTGACATTACCAAACTGCTCCTGGCTGTTTGGCCCT

HepCla #146

HepCla #78

S P R P I S Y L K G S S G G P L L C P A G H A V G I F R A A AGCCCTAGGCCTATCTCCTACCTCAAGGGAAGCTCCGGCGGACCCCTCCTGTGTCCCGCTGGCCATGCCGTCGGCATTTTCAGAGCCGCT

HepCla #32

D F D Q G W G P I S Y A N G S G P D Q R P Y C W H Y P P K P GACTTTGACCAAGGCTGAGGCCTATCTCCTACGCTAACGGAAGCGGACCCGATCAGAGACCCTATTGCTGGCACTATCCCCCTAAGCCT

HepCla #128

R H V G P G E G A V Q W M N R L I A F A S R G N H V S P T H
AGGCATGTGGGACCCGGAGAGGGAGCCGTCCAGTGGATGAATAGGCTCATCGCTTTCGCTAGCAGAGGCAATCACGTCAGCCCTACCCAT

HepCla #50

C L W M M L L I S Q A E A A L E N L V I L N A A S L A G T H
TGCCTCTGGATGATGCTCCTGATTAGCCAAGCCGAAGCCGTCTGGAAAACCTCGTGATTCTGAATGCCGCTAGCCTCGCCGGAACCCAT

HepC1a #114

I I P D R E V L Y R E F D E M E E C S Q H L P Y I E Q G M M ATCATTCCCGATAGGGAAGTGCTCTACAGAGAGTTTGACGAAATGGAAGAGTGTAGCCAACACCTCCCCTATATCGAACAGGGAATGATG

HepCla #47

f L I H L H Q N I V D V Q Y L Y G V G S S I A S W A I .K W E Y CTGATTCACCTCCACCAAAACATTGTGGATGTGCAATACCTCTACGGAGTGGGAAGCTCCATCGCTAGCTGGGCCATTAAGTGGGAGTAT

HepCla #200

 $oldsymbol{^{'}}$ S H A R P R W F W F C L L L A A G V G I Y L L P N R A A GTGTCCCACGCTAGGTGGTTCTGGTTCTGCTCCTGCTGGCCGCTGGCGTTTACCTCCTGCCTAACAGAGCCGCT

HepCla #85

HepCla #62

R V Q G L L R I C A L A R K M I G G H Y V Q M A I I K L G A AGGGTCCAGGGACTCCTCAGGATTTGCGCTCTGGCTAGGAAAATGATTGGCGACACTATGTGCAAATGGCTATCATTAAGCTCGGCGCT

HepCla #153

R R F A Q A L P V W A R P D Y N P P L V E T W K K P D Y E P AGGAGATTCGCTCAGGCTCTGCCTGTGTGGGGCCAGACCCGATTACAATCCCCCTCTGGTCGAGACATGGAAAAAGCCTGACTATGAGCCT

HepCla #72

T A A Q T F L A T C I N G V C W T V Y H G A G T R T I A S P ACCGCTGCCCAAACCTTTCTGGCTACCAATGGCGTCTGCTGGACCGTCTACCATGGCGCTCTGCCAAGGACAATCGCTAGCCCT

HepCla #65

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HepCla #74

K G P V I Q M Y T N V D Q D L V G W P A P Q G S R S L T P C AAGGGACCCGTCATCCAAATGTATACCAATGTGGATCAGGATCTGGTCGGCTGGCCCGCTCCCCAAGGCTCCCAGGTCCCTGACACCCTGT

HepC1a #151

K V V I L D S F D P L V A E E D E R E I S V P A E I L R K S AAGGTCGTGATTCTGGATAGCCTCTGGTCGCCGAAAGGTCC

HepCla #64

L T G T Y V Y N H L T P L R D W A H N G L R D L A V A V E P CTGACAGGCACATACGGCACTACAGCCTCTGAGAGACCTCGAGCCTCTGAGAGACCTCGCCGTCGAGCCCT

HepCla #80

f V C f T R G f V A f K A f V D F f I P f V E N f L E f T f T M R S P f V F f T D N GTGTGTACCAGAGGCGTCGCCAAAGCCGTCGTCTTCACAGACAAT

HepCla #95

A L G I N A V A Y Y R G L D V S V I P T S G D V V V V A T D GCCCTCGGCATTAACGCTGTGGCTTACTATAGGGGACTGGATGTGCCGTGATTCCCACAAGCGGAGACGTCGTGGTCGTGGCTACCGAT

HepCla #111

M S A D L E V V T S T W V L V G G V L A A L A A Y C L S T G ATGTCCGCCGATCTGGAAGTGGTCACCTCGACCTGGGTGCTCGTGGGAAGTGGTCACCTCACCGGA

HepCla #97

A L M T G Y T G D F D S V I D C N T C V T Q T V D F S L D P GCCCTCATGACAGGCTATACCGGAGACTTTGACTCCGTGATTGACTGTAACACATGCGTCACCCAAACCGTCGACTTTAGCCTCGACCCT

HepCla #2

N T N R R P Q D V K F P G G G Q I V G G V Y L L P R R G P R AACACAAACAGAAGGCCTCAGGATGTGAAATTCCCTGGCGGAGGCCAAATCGTCGGCGGAGTGTATCTGCTCCCCAGAAGGGGACCCAGA

HepCla #11

R[®] A L A H G V R V L E D G V N Y A T G N L P G C S F S I F L AGGGCTCTGGCTCACGAGGAGTGAGGATGCCTCAACTATGCCACAGGCAATCTGCCTGGCTGAGCTTTAGCATTTTCCTC

HepCla #169

S K F G Y G A K D V R C H A R K A V A H I N S V W K D L L E AGCAAATTCGGATACGGAGCCAAAGACGTCAGGTGTCACGCTAGGAAAGCCGTCGCCCATATCAATAGCGTCTGGAAAGACCTCCTGGAA

HepCla #28

 $ilde{ t T}$ P $ilde{ t G}$ A K Q N I Q L I N T N G S W H I N S T A L N C N E S L ACCCCTGGCGCTAAGCAAAACATTCAGCTCAATACCAATGGCTCCTGGCATATCAATAGCACAGCCCTCAACTGTAACGAAAGCCTC

HepCla #30

N T G W L A G L F Y Q H K F N S S G C P E R L A S C R R L T AACACAGGCTGGCTGGCTGTCTTCTATCAGCATAAGTTTAACTCCAGCGGATGCCTGAGAGACTGGCTAGCTGTAGGAGACTGACA

HepCla #49

HepCla #192

D C E I Y G A C Y S I E P L D L P P I I Q R L H G L S A F S GACTGTGAGATTTACGGAGCCTGTTACTCCATCGAACCCCTCGACCTCCCCCCTATCATTCAGAGACTGCATGGCCTCAGCGCTTTCTCC

HepCla #73

W T V Y H G A G T R T I A S P K G P V I Q M Y T N V D Q D L TGGACAGTGTATCACGGAGCCGGAACCAGAACCATTGCCTCCCCCAAAGGCCCTGTGATTCAGATGTACACAAACGTCGACCAAGACCTC

HepCla #101

Y R F V A P G E R P S G M F D S S V L C E C Y D A G C A W Y TACAGATTCGTCGCCCCTGGCGAAAGGCCTAGCGGAATGTTTGACTCCAGCGTCCTGTGTGAGTGTTACGATGCCGGATGCGCTTGGTAT

HepCla #45

R S E L S P L L S T T Q W Q V L P C S F T T L P A L S T G
AGGTCCGAGCTCAGCCCTCTGCTCCACCACACAGTGGCAGGTCCTGCCTTGCTCCTTCACAACCCTCCCCGCTCTGTCCACCAGGA

HepCla #195

L R K L G V P P L R A W R H R A R S V R A R L L A R G G R A

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HepCla #121

S P L T T S Q T L L F N I L G G W V A A Q L A A P G A A T A AGCCCTCTGACACCTCCCGGACCTCTCAATATCCTCGGCGGATGGGTCGCCGCTCAGCTCGCCGCTCCCGGAGCCGCTACCGCT

HepCla #61

L W I L Q A S L L K V P Y F V R V Q G L L R I C A L A R K M CTGTGGATCCTCCAGGCTAGCCTCCTGAAAGTGCCTTGTGAAAGTTG

HepC1a #137

V K N G T M R I V G P R T C R N M W S G T F P I N A Y T T G GTGAAAAACGGAACCATGAGGATTGTGGGACCCAGAACCTGTAGGAATATGTGGAGCGGAACCTTTCCCATTAACGCTTACACAACCGGA

HepC1a #92

E V A L S T T G E I P F Y G K A I P L E V I K G G R H L I F GAGGTCGCCTCAGCAACCGGAGAGATTCCCTTTTACGGAAAGGCTATCCCTCTGGAAGTGATTAAGGGAGGAGACACCTCATCTTT

HepCla #188

 $ilde{\mathbf{L}}$ T R D P T T P L A R A A W E T A R H T P V N S W L G N I I CTGACAAGGGATCCCACACCCCTCGGCTAGGGCTAGGCCTGGGAGACACCACACCCCGTCAACTCCTGGCTAGATATCATT

HepC1a #140

R V S A E E Y V E I R R V G D F H Y V T G M T T D N L K C P AGGGTCAGCGCTGAGAATACGTCGAGATTAGGAGAGTGGGAGACTTTCACTATGTGACAGGCATGACCACAGACAATCTGAAATGCCCT

HepCla #155

PVVHGCPLPPPRSPPVPPRKKRTVVLTES
CCCGTCGTGCATGGCTGCCCCCCCCCCCCAGAAGGACAGAGGACAGTGGTCCTGACAGAGTCC

HepCla #157

T L S T A L A E L A T K S F G S S T S G I T G D N T T T S ACCCTCAGCACAGCCCTCCGCAACTGCCTACCAAAAGCTTTGGCTCCAGCTCCACCTCCGGCATTACCGGAGACAATACCACAACCTCC

HepCla #135

HepCla #20

V F L V G Q L F T F S P R R H W T T Q G C N C S I Y P G H I GTGTTTCTGGTCGGCCAACTGTTTACCTTTAGCCCTAGGAGACACTGGACCACACAGGGATGCCAATTGCTCCATCTATCCCGGACACATT

HepCla #123

F V G A G L A G A A I G S V G L G K V L V D I L A G Y G A G TTCGTCGGCGCTCGCCGGAGCCGCTATCGGAAGCGTCGGCCTCGGCAAAGTGCTCGTGGATATCCTCGCCGGATACGGAGCCGGA

HepCla #133

D I W D W I C E V L S D F K T W L K A K L M P Q L P G I P F GACATTTGGGATTTGCGAAGTGCTCAGCGATTCCCTTT

HepCla #15

N S S I V Y E A A D A I L H T P G C V P C V R E G N A S R C AACTCCAGCATTGTGTATGAGGCTGCCGATGCCATCTGCATACCCCTGGCTGTGTGCCTTGCGTCAGGGAAGGCAATGCCTCCAGGTGT

HepCla #31

S S G C P E R L A S C R R L T D F D Q G W G P I S Y A N G S AGCTCCGGCTGTCCCGAAAGGCTCCTGCAGAAGGCTCACCGATTTCGATCAGGGATGGGACCCATTAGCTATGCCAATGGCTCC

HepCla #178

HepCla #69

V S K G W R L L A P I T A Y A Q Q T R G L L G C I I T S L T GTGTCCAAGGGATGGAGACTGCTCGCCCTATCACAGCCTATGCCCAACAGACAAGGGGACTGCTCGGCTGTATCATTACCTCCCTGACA

HepCla #191

F F S V L I A R D Q L E Q A L D C E I Y G A C Y S I E P L D TTCTTTAGCGTCCTGATTGCCAGAGACCACTGGAACAGGCTCTGGATTGCGAAATCTATGGCGCTTGCTATAGCATTGAGCCTCTGGAT

HepCla #142

C Q V P S P E F F T E L D G V R L H R F A P P C K P L L R E TGCCAAGTGCCTAGCCTGAGGTTTTCACAGAGCTCGACGGAGTGAGACTGCATAGGTTTGCCCCTCCTGTAAGCCTCTGCTCAGGGAA

140/216

HepCla #182

T C Y I K A R A A C R A A G L Q D C T M L V C G D D L V V I ACCTGTTACATTAAGGCTAGGGCTGCGTGAGGCTGCCGGACTGCAAGACTGTACCATGCTGGTCTGCGGAGACGATCTGGTCGTGATT

HepCla #86

HepCla #44

HepCla #22

 $ar{ extsf{T}}$ G H R M A W D M M N N S P T A A L V M A Q L L R I P Q A ACCGGACACAGAATGGCTTGGGATATGATGATGATGATTGGTCCCCCACAGCCGCTCTGGTCATGGCTCAGCTCTGAGAATCCCTCAGGCT

HepCla #127

P G A L V V G V V C A A I L R R H V G P G E G A V Q W M N R CCCGGAGCCCTCGTGGTGGGTGTGTGCGCTTTCCTCAGGAGACACGTCGGCCCTGGCGAAGGCGCTGTGCAATGGATGAACAGA

HepCla #149

H D S P D A E L I E A N L L W R Q E M G G N I T R V E S E N CACGATAGCCCTGACGCTCATCGAAGCCAATCTGCTCTGGAGACAGGAAATGGGAGACAATATCACAAGGGTCGAGTCCGAGAAT

HepCla #105

HepCla #5

R G R R Q P I P K A R R P E G R T W A Q P G Y P W P L Y G N AGGGGAAGGACCTGAGCAGACCTGGATACCCTTGGCCTCTGTATGGCAAT

HepCla #173

L I V F P D L G V R V C E K M A L Y D V V S K L P L A V M G CTGATTGTGTTTCCCGATCTGGGAGTGAGAGTGTGTGAGAAAATGGCTCTGTATGACGTCGTGTCCAAGCTCCCCTCGCCGTCATGGGA

HepCla #12

HepCla #124

L G K V L V D I L A G Y G A G V A G A L V A F K I M S G E V CTGGGAAAGGTCCTGGTCGAAAATCATGAGCGGAGAGGTC

Wencia #160

S Y S S M P P L E G E P G D P D L S D G S W S T V S S E A G AGCTATAGCTCCATGCCTCCCCTCGAGGGAGGCCTGGCGATCCCGATCTCTCCGACGGAAGCTGGAGCACAGTGTCCAGCGAAGCCGGA

HepCla #150

R Q E M G G N I T R V E S E N K V V I L D S F D P L V A E E AGGCAAGAGTGGGCAACACTCCTCGACCCCTCGTGGCTGAGGAA

HenCla #75

V G W P A P Q G S R S L T P C T C G S S D L Y L V T R H A D GTGGGATGCCTCTCCTCAGGGAAGCCTCACCCCTTGCACATGCGGAAGCTCCGACCTCTACCTCGTGACAAGGCATGCCGAT

HepCla #88

G C S G G A Y D I I I C D E C H S T D A T S I L G I G T V L GGCTGTAGCGGAGGCGCTTACGATATCATTATCTGTGACGAATGCCATAGCACAGACGCTACCTCCATCCTCGGCATTGGCACAGTGCTC

HepCla #99

 $ilde{ t T}$ F T I E T T T L P Q D A V S R T Q R R G R T G R G K P G I ACCTTTACCATTGAGACCACACCACACGGAAGCCTGGCATT

HepCla #40

D C F R K H P E A T Y S R C G S G P W I T P R C L V D Y P Y GACTGTTTCAGAAAGCATCCCGAAGCCACATACTCCAGGTGTGGCTCCGGCCCTTGGATTACCCCTAGGTGTCTGGTCGACTATCCCTAT

HepCla #201

LAAGVGIYLLPNRAA CTGGCTGCCGGAGTGGGAATCTATCTGCTCCCCAATAGGGCTGCC

141/216

HepCla #163

A L V T P C A A E E Q K L P I N A L S N S L L R H H N L V Y GCCCTCGTGACACCCTGAGGAACAGAAACTGCCTATCAATGCCTCAGGAATAGCCTCCTGAGACACCATAACCTCGTGTAT

HepC1a #132

ISSECTTPCSGSWLRDIWDWICEVLSDFKTATCTCCAGCGAATGCACACCCCTTGCTCCGGCTCCTGGCTCAGGGATATCTGGGACTGGATCTGTGAGGTCCTGTCCGACTTTAAGACA

HepCla #134

W L K A K L M P Q L P G I P F V S C Q R G Y K G V W R G D G TGGCTCAAGGCTAAGCCTCAGCTCCCCGGAATCCCTTTCGTCAGCTGTCAGAGAGGCTATAAGGGAGTGTGGAGGGGAGACGGA

HepCla #41

S G P W I T P R C L V D Y P Y R L W H Y P C T I N Y T I F K
AGCGGACCCTGGATCACACCCAGATGCCTCGGGATTACCTTACCATTACCATTTTCAAA

Artificial Protein:

 ${\tt VIPVRRRGDSRGSLLSPRPISYLKGSSGGPARRGREILLGPADGMVSKGWRLLAPITAYARLHRFAPPCKPLLREEVSFRVGLHEYPVGSVVFSQMET}$ KLITWGADTAACGDIINGLPVSLLCPAGHAVGIFRAAVCTRGVAKAVDFIPVCVVIVGRIVLSGKPAIIPDREVLYREFDEMPCTPLPAPNYTFALWR VSAEEYVEIRRVGDALYDVVSKLPLAVMGSSYGFQYSPGQRVEFISWCLWWLQYFLTRVEAQLHVWVPPLNVRGENLVILNAASLAGTHGLVSFLVFF CFAWYLLPPIIQRLHGLSAFSLHSYSPGEINRVAACNPPLVETWKKPDYEPPVVHGCPLPPPRSPPGVGSSIASWAIKWEYVVLLFLLLADARVCSLN NTRPPLGNWFGCTWMNSTGFTKVCGAPPFTEAMTRYSAPPGDPPQPEYDLELITSCSSWPLLLLLLALPQRAYALDTEVAASCGGVVLQQTRGLLGCI ITSLTGRDKNQVEGEVQIVSSSPPAVPQSFQVAHLHAPTGSGKSTKVPAANTPGLPVCQDHLEFWEGVFTGLTHIDAHFLVLLLFAGVDAETHVTGGN AGRTTSGLVSLLEVTLITHPVTKYIMTCMSADLEVVTSTWVLVVGLMALTLSPYYKRYISWCLWWLQYFLTRVAICGKYLFNWAVRTKLKLTPIAAAGR LDLS1AYFSMVGNWAKVLVVLLLFAGVDAETHVTRLARGSPPSMASSSASQLSAPSLKATCTANGLVSFLVFFCFAWYLKGRWVPGAVYALYGMQLPC EPEPDVAVLTSMLTDPSHITAEAAGRDSVTPIDTTIMAKNEVFCVQPEKGGRKPARYAAQGYKVLVLNPSVAATLGFGAYMSKAHGVRNSTGLYHVTN ${\tt DCPNSSIVYEAADAILHTSSYGFQYSPGQRVEFLVQAWKSKKTPMGFSDTAACGDIINGLPVSARRGREILLGPADGMSQLSAPSLKATCTANHDSPD$ AELIEANLLWNPAIASLMAFTAAVTSPLTTSQTLLFNILGLVQAWKSKKTPMGFSYDTRCFDSTVTESDIDEREISVPAEILRKSRRFAOALPVWARP DYMFAPTLWARMILMTHFFSVLIARDQLEQALSVIPTSGDVVVVATDALMTGYTGDFDSVIDCHSKKKCDELAAKLVALGINAVAYYRGLDVVLPCSF TTLPALSTGLIHLHQNIVDVQYLYKGRWVPGAVYALYGMWPLLLLLLALPQRAYSPITYSTYGKFLADGGCSGGAYDIIICDECARSVRARLLARGGR AAICGKYLFNWAVRTKKAVAHINSVWKDLLEDSVTPIDTTIMAKNEFTPSPVVVGTTDRSGAPTYSWGANDTDVFVPGCVPCVREGNASRCWVAMTPT VATROGKLQDCTMLvCGDDLvVICESAGvQEDAASLRAVAGALvAFKIMSGEvpsTedLvnLlpailsydtrcfdstvtesdirteeaiyqccdldpq ELTPAETTVRLRAYMNTPGLPVCQDHLEFWPQPEYDLELITSCSSNVSVAHDGAGKRVYYLGKVIDTLTCGFADLMGYIPLVGAPLGGAAAIPLEVIK GGRHLIFCHSKKKCDELAAKLVGGVLAALAAYCLSTGCVVIVGRIVLSGKPACESAGVQEDAASLRAFTEAMTRYSAPPGDPGWFTAGYSGGDIYHSV DLEDRDEAQLHVWVPPLNVRGGRDAVILLMCVVHPTLGVRATRKTSERSQPRGRRQPIPKARRPEGNVSVAHDGAGKRVYYLTRDPTTPLARAAWESE PAPSGCPPDSDAESYSSMPPLEGEPGDPIGGHYVQMAIIKLGALTGTYVYNHLTPLRDPSTEDLVNLLPAILSPGALVVGVVCAAILRILDMIAGAHW GVLAGIAYFSMVGNWAKVLVEGCGWAGWLLSPRGSRPSWGPTDPRRRSRNWTTQGCNCSIYPGHITGHRMAWDMMMNWSPWVAMTPTVATRDGKLPAT QLRRHIDLLVGSRLWHYPCTINYTIFKVRMYVGGVEHRLEAAVFCVQPEKGGRKPARLIVFPDLGVRVCEKMMGYIPLVGAPLGGAARALAHGVRVLE DGVNGGNAGRTTSGLVSLLTPGAKQNIQLINTNGLALLSCLTVPASAYQVRNSTGLYHVTNDCPGRDKNQVEGEVQIVSTAAQTFLATCINGVCPATQ LRRHIDLLVGSATLCSALYVGDLCGSHAPTGSGKSTKVPAAYAAQGYKVLVLNPSVRTWAQPGYPWPLYGNEGCGWAGWLLSPRGSTEDVVCCSMSYS WTGALVTPCAAEEQKLPIALDTEVAASCGGVVLVGLMALTLSPYYKRYWMNSTGFTKVCGAPPCVIGGAGNNTLHCPTSVEEACSLTPPHSAKSKFGY GAKDVRCHARISGIQYLAGLSTLPGNPAIASLMAFTAAVTQIVGGVYLLPRRGPRLGVRATRKTSERSQPLHSYSPGEINRVAACLRKLGVPPLRAWR ${\tt HRTARHTPVNSWLGNIIMFAPTLWARMILMTHENLETTMRSPVFTDNSSPPAVPQSFQVAHLATPPGSVTVPHPNIEEVALSTTGEIPFYGKLVFDIT$ KLLLAVFGPLWILQASLLKVPYFVTAALVMAQLLRIPQAILDMIAGAHWGVLAGCNTCVTQTVDFSLDPTFTIETTTLPQDAVSHGPTPLLYRLGAVQ NEVTLTHPVTKYIMTCARVAIKSLTERLYVGGPLTNSRGENCGYRRCVIGGAGNNTLHCPTDCFRKHPEATYSRCGTCGSSDLYLVTRHADVIPVRRR GDSRGSLLNMWSGTFPINAYTTGPCTPLPAPNYTFALWHSTDATSILGIGTVLDQAETAGARLVVLATYVPESDAAARVTAILSSLTVTOLLRRLHOW RPSWGPTDPRRRSRNLGKVIDTLTCGFADLGPDQRPYCWHYPPKPCGIVPAKSVCGPVYCEECSQHLPYIEQGMMLAEQFKQKALGLLQTYQATVCAR AQAPPPSWDQMWKCLIRLKPTLCGIVPAKSVCGPVYCFTPSPVVVGTTDRSGSSLTVTQLLRRLHQWISSECTTPCSGSWLRDLSDGSWSTVSSEAGT EDVVCCSMSYSWTGWDQMWKCLIRLKPTLHGPTPLLYRLGAVQNLAEQFKQKALGLLQTASRQAEVIAPAVQTNWQKLEVFWAKHMWNFISGIQYLAG LSTLPGLIAFASRGNHVSPTHYVPESDAAARVTAILATLCSALYVGDLCGSVFLVGQLFTFSPRRHSSVLCECYDAGCAWYELTPAETTVRLRAYMGW VAAQLAAPGAATAFVGAGLAGAAIGSVGSWHINSTALNCNESLNTGWLAGLFYQHKFNNALSNSLLRHHNLVYSTTSRSACQRQKKVTAAMSTNPKPQ RKTKRNTNRRPQDVKFPGGGSQTKQSGENFPYLVAYQATVCARAQAPPPSAPTYSWGANDTDVFVLNNTRPPLGNWFGCTVPPPRKKRTVVLITESTLS ${\tt TALAELATKSFGSTTSRSACQRQKKVTFDRLQVLDSHYQDVLDQAETAGARLVVLATATPPGSVTVPHPN1EFHYVTGMTTDNLKCPCQVPSPEFFTE}$ QVLDSHYQDVLKEVKAAASKVKANLLGPLTNSRGENCGYRRCRASGVLTTSCGNTLIMHTRCHCGAEITGHVKNGTMRIVGPRTCREVSFRVGLHEYP vgsqlpcepepdvavltskevkaaaskvkanllsveeacsltpphsakgrdavillmcvvhptlvfditkllavfgpmltdpshitaeaagrrlarg SPPSMASSSASPRPISYLKGSSGGPLLCPAGHAVGIFRAADFDQGWGPISYANGSGPDQRPYCWHYPPKPRHVGPGEGAVQWMNRL1AFASRGNHVSP $\texttt{THCLWMMLLISQAEAALENLVILNAASLAGTHIIPDREVLYREFDEMEECSQHLPYIEQGMMLIHLHQNIVDVQYLYGVGSSIASWAIKWEYVSHARPICARREALENLVILNAASLAGTHIIPDREVLYREFDEMEECSQHLPYIEQGMMLIHLHQNIVDVQYLYGVGSSIASWAIKWEYVSHARPICARREALENLVILNAASLAGTHIIPDREVLYREFDEMEECSQHLPYIEQGMMLIHLHQNIVDVQYLYGVGSSIASWAIKWEYVSHARPICARREALENLVILNAASLAGTHIIPDREVLYREFDEMEECSQHLPYIEQGMMLIHLHQNIVDVQYLYGVGSSIASWAIKWEYVSHARPICARREALENLVILNAASLAGTHIIPDREVLYREFDEMEECSQHLPYIEQGMMLIHLHQNIVDVQYLYGVGSSIASWAIKWEYVSHARPICARREALENLVILNAASLAGTHIIPDREVLYREFDEMEECSQHLPYIEQGMMLIHLHQNIVDVQYLYGVGSSIASWAIKWEYVSHARPICARREALENLVILNAASLAGTHIIPDREVLYREFDEMEECSQHLPYIEQGMMLIHLHQNIVDVQYLYGVGSSIASWAIKWEYVSHARPICARREALENLVILNAASLAGTHIIPDREVLYREFDEMEECSQHLPYIEQGMMLIHLHQNIVDVQYLYGVGSSIASWAIKWEYVSHARPICARREALENLVILNAASLAGTHIIPDREVLYREFDEMEECSQHLPYIEQGMMLIHLHQNIVDVQYLYGVGSSIASWAIKWEYVSHARPICARREALENLVILNAASLAGTHIIPDREVLYREFDEMEECSQHLPYIEQGMMLIHLHQNIVDVQYLYGVGSSIASWAIKWEYVSHARPICARREALENLVILNAASLAGTHIIPDREVLYREFDEMEECSQHLPYIEQGMMLIHLHQNIVDVQYLYGVGSSIASWAIKWEYVSHARPICARREALENLVILNAASLAGTHIIPDREVLYREFDEMEECSQHLPYIEQGMMLIHLHQNIVDVQYLYGVGSSIASWAIKWEYVSHARPICARREALENLVILNAASLAGTHIIPDREVLYREFDEMEECSQHLPYIEQGMMLIHLHQNIVDVQYLYGVGSSIASWAIKWEYVSHARPICARREALENLVILNAASLAGTHIIPDREVLYREFDEMEECSQHLPYIEQGMMLIHLHQNIVDVQUTARREALENLVILNAASLAGTHIIPDREVLYREFDEMEECSQHLPYIEQGMMLIHLHQNIVDVQUTARREALENLVILNAASLAGTHIIPDREVLYREFDEMEECSQHLPYIEQGMMLIHLHQNIVDVQUTARREALENLVILNAASLAGTHIIPDREVLYREFTUR ALIFFICARREALENLVILNAASLAGTHIIPDREVLYREFTUR ALIFFICARREALENLVILNAASLAG$ RWFWFCLLLLAAGUGIYLLPNRAAAATLGFGAYMSKAHGIDPNIRTGVRTITTGRVQGLLRICALARKMIGGHYVQMAIIKLGARRFAQALPVWARPDYNPPLVETWKKPDYEPTAAQTFLATCINGVCWTVYHGAGTRTIASPWAHNGLRDLAVAVEPVVFSQMETKLITWGAKGPVIQMYTNVDQDLVGWPAPQ GSRSLTPCKVVILDSFDPLVAEEDEREISVPAEILRKSLTGTYVYNHLTPLRDWAHNGLRDLAVAVEPVCTRGVAKAVDFIPVENLETTMRSPVFTDN $\textbf{ALGINAVAYYRGLDVSVIPTSGDVVVVATDMSADLEVVTSTWVLVGGVLAALAAYCLSTGALMTGYTGDFDSVIDCNTCVTQTVDFSLDPNTNRRPQD$ VKFFGGGQIVGGVYLLPRRGPRRALAHGVRVLEDGVNYATGNLPGCSFSIFLSKFGYGAKDVRCHARKAVAHINSVWKDLLETPGAKONIOLINTNGS WHINSTALNCNESLNTGWLAGLFYQHKFNSSGCPERLASCRRLTVVLLFLLLADARVCSCLWMMLLISQAEAALDCEIYGACYSIEPLDLPPIIQRLH GLSAFSWTVYHGAGTRTIASPKGPVIQMYTNVDQDLYRFVAPGERPSGMFDSSVLCECYDAGCAWYRSELSPLLLSTTQWQVLPCSFTTLPALSTGLR KLGVPPLRAWRHRARSVRARLLARGGRASPLTTSQTLLFNILGGWVAAQLAAPGAATALWILQASLLKVPYFVRVQGLLRICALARKMVKNGTMRIVG PRTCRNMWSGTFPINAYTTGEVALSTTGEIPFYGKAIPLEVIKGGRHLIFLTRDPTTPLARAAWETARHTPVNSWLGNIIRVSAEEYVEIRRVGDFHY ${\tt VTGMTTDNLKCPPVVHGCPLPPPRSPPVPPPRKKRTVVLTESTLSTALAELATKSFGSSSTSGITGDNTTTSVSCQRGYKGVWRGDGIMHTRCHCGAE$ ITGHVFLVGQLFTFSPRRHWTTQGCNCSIYPGHIFVGAGLAGAAIGSVGLGKVLVDILAGYGAGDIWDWICEVLSDFKTWLKAKLMPQLPGIPFNSSI VYEAADAILHTPGCVPCVREGNASRCSSGCPERLASCRRLTDFDQGWGPISYANGSRTEEAIYQCCDLDPQARVAIKSLTERLYVGVSKGWRLLAPIT AYAQQTRGLLGCIITSLTFFSVLIARDQLEQALDCEIYGACYSIEPLDCQVPSPEFFTELDGVRLHRFAPPCKPLLRETCYIKARAACRAAGLQDCTM

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LVCGDDLVVIIDPNIRTGVRTITTGSPITYSTYGKFLADGCNWTRGERCDLEDRDRSELSPLLLSTTQWQTGHRMAWDMMMNWSPTAALVMAQLLRIP QAPGALVVGVVCAAILRRHVGPGEGAVQWMNRHDSPDAELIEANLLWRQEMGGNITRVESENEGVFTGLTHIDAHFLSQTKQSGENFPYLVARGRRQP IPKARRPEGRTWAQPGYPWPLYGNLIVFPDLGVRVCEKMALYDVVSKLPLAVMGYATGNLPGCSFSIFLLALLSCLTVPASAYQLGKVLVDILAGYGA GVAGALVAFKIMSGEVSYSSMPPLEGEPGDPDLSDGSWSTVSSEAGRQEMGGNITRVESENKVVILDSFDPLVAEEVGWPAPQGSRSLTPCTCGSSDL YLVTRHADGCSGGAYDIIICDECHSTDATSILGIGTVLTFTIETTTLPQDAVSRTQRRGRTGRGKPGIDCFRKHPEATYSRCGSGPWITPRCLVDYPY LAAGVGIYLLPNRAAALVTPCAAEEQKLPINALSNSLLRHNLVYISSECTTPCSGSWLRDIWDWICEVLSDFKTWLKAKLMPQLPGIPFVSCQRGYK GVWRGDGSGPWITPRCLVDYPYRLWHYPCTINYTIFK

Artificial DNA:

 ${\tt GGGAAGGGAAATCCTCCTGGGACCCGCTGACGGAATGGTCAGCAAAGGCTGGAGGCTCCTGGCTCCCATTACCGCTTACGCTTACGCTCCACAGATTCGCTCACAGATTCGCTACGCTCACAGATTCGCTACGCTCACAGATTCGCTACGCTCACAGATTCGCTACGCTACGCTCACAGATTCGCTACGCTACAGATTCGCTACAGATTCGCTACAGATTCGCTACGCTACAGATTCGCTACAGATTCACAGATTCGCTACAGATTCGCTACAGATTCGCTACAGATTCGCTACAGATTCGCTACAGATTCGCTACAGATTCGCTACAGATTCGCTACAGATTCGCTACAGATTCGCTACAGATTCGCTACAGATTCACAGATTCGCTACAGATTCGCTACAGATTCGCTACAGATTCGCTACAGATTCGCTACAGATTCACAGATTCGCTACAGATTCGCTACAGATTCGCTACAGATTCGCTACAGATTCGCTACAGATTCGCTACAGATTCGCTACAGATTCGCTACAGATTCGCTACAGATTCGCTACAGATTCA$ $\tt CTCCCCCTTGCAAACCCCTCCTGAGAGGGAAGTGTCCTTCAGAGTGGGACTGCATGAGTATCCCGTCGGCTCCGTGGTCTTCTCCCAGATGGAGACA$ AAGCTCATCACATGGGGAGCCGATACCGCTGCCTGTGGCGATATCATTAACGGACTGCCTGTGTCCCTGCCCTGCCCGGACACGCTGTGGGAAT $\tt GTGTCCGCCGAAGAGTATGTGGAAATCAGAAGGGTCGGCGATGCCCTCTACGATGTGGTCAGCAAACTGCCTCTGGCTGTGATGGGCTCCAGCTATGG$ ${\tt TGCT}{\tt TTGCCTGGTACCTCCCTGCCTCCCATTATCCAAAGGCTCCACGGACTGTCCGCCTTTAGCCTCCACTCCTACTCCCCCGGAGAGATTAACAGAGT$ $\operatorname{\mathsf{GGCT}}$ ${ t CTGGCGTCGGCTCCAGCATTGCCTCCTGGGCTATCAAATGGGAATACGTCGTGCTCCTGTTTCTGCTCCTGGCTGACGCTAGGGTCTGCTCCCTGAAT$ ${\tt AACACAAGGCCTCCCCTCGGCAATTGGTTTGGCTGTACCTGGATGAATAGCACAGGCTTTACCAAAGTGTGTGGCGCTCCCCCTTTCACAGAGGCTAT}$ ${\tt GACAAGGTATAGCGCTCCCCCTGGCGATCCCCCTCAGCCTGAGTATGACCTCGAGCTCATCACAAGCTGTAGCTCCTGGCCTCTGCTCCTGCTCCTGC$ AAGGCGTCTTCACAGGCCTCACCCATATCGATGCCCATTTCCTCGTGCTCCTGCTCTTCGCTGGCGTCGACGCTGAGACACACGTCACCGGAGGCAAT ${\tt GGTCGTGACAAGCACATGGGTCGTGGGGACTGATGGCCCTCACCCTCAGCCCTTACTATAAGAGATACATTAGCTGGTGCCTCTGGTGGCTGC$ ${\tt AATACTTTCTGACAAGGGTCGCCATTTGCGGAAAGTATCTGTTTAACTGGGCCGTCAGGACAAAGCTCAAGCTCACCCCTATCGCTGCCGCTGGCAGA$ $\tt CTGGATCTGTCCATCGCTTACTTTAGCATGGTGGGAAACTGGGCCAAAGTGCTCGTGGTCCTGTTTGCCGGAGTGGATGCCGAAACCCATGT$ ${\tt TCGTGTCCTTCGTGTTTTCTGTTTCGCTTGGTATCTGAAAGGCAGATGGGTCCCCGGAGCCGTCTACGCTCTGTATGGCATGCAGCTCCCCTGT$ GAGCCTGAGCCTGACGTCGCCGTCCTGACAAGCATGCTGACAGACCCTAGCCATATCACAGCCGAAGCCGCTGGCAGAGACTCCGTGACACCCATTGA ${\tt CACAACCATTATGGCTAAGAATGAGGTCTTCTGTGTGCAACCCGAAAAGGGAGGCAGAAAGCCTGCCAGATACGCTGCCCAAGGCTATAAGGTCCTGG}$ ${ t TCCTGAATCCCTCCGTGGCTGCCACACTGGGATTCGGAGCCTATATGTCCAAGGCTCACGGAGTGAGAAACTCCACCGGACTGTATCACGTCACCAAT$ GACTGTCCCAATAGCTCCATCGTCTACGAAGCCGCTGACGCTATCCTCCACACAAGCTCCTACGGATTCCAATACTCCCCCGGACAGAGAGTGGAATT CCTCGTGCAAGCCTGGAAGTCCAAGAAAACCCCTATGGGATTCTCCGACACAGCCGCTTGCGGAGACATTATCAATGGCCTCCCCGTCAGCGCTAGGA AAAAGAAATGCGATGAGCTCGCCGCTAAGCTCGTGGCTCTGGGAATCAATGCCGTCGCCTATTACAGAGGCCTCGACGTCGTGCTCCCCTGTAGCTTTGTATGCCCTCTACGGAATGTGGCCCCTCCTGCTCCTGCTCCTGCTCCTGCCTCAGAGAGCCCTATAGCCCTATCACATACTCCACCTATGGCAAATTCC TCGCCGATGCCGGATGCTCCGGCGGAGCCTATGACATTATCATTTGCGATGAGTGTGCCAGAAGCGTCAGGGCTAGGCTAGGCGAGGCAGA ${\tt GCCGCTATCTGTGGCAAATACCTCTTCAATTGGGCTGTGAGAACCAAAAAGGCTGTGGCTCACATTAACTCCGTGTGGAAGGATCTGCTCGAGGATAG}$ CGTCACCCCTATCGATACCACAATCATGGCCAAAAACGAATTCACACCCTCCCCGTCGTCGTCGGCACAACCGATAGGTCCGGCGCTCCCACATACT $\tt GTGGCTACCAGAGACGGAAAGCTCCAGGATTGCACAATGCTCGTGTGTGGCGATGACCTCGTGGTCATCTGTGAGTCCGCCGGAGTGCAAGAGGATGC$ GAGCTCACCCCTGCCGAAACCACAGTGAGACTGAGAGCCTATATGAATACCCCTGGCCTCCCCGTCTGCCAAGACCATCTGGAATTCTGGCCCCAACC CGAATACGATCTGGAACTGATTACCTCCTGCTCCAGCAATGTGTCCGTGGCTCACGATGGCGCTGGCAAAAGGGTCTACTATCTGGGAAAGGTCATCG $\tt ATACCCTCACCTGTGGCTTTGCCGATCTGATGGGCTATATCCCTCTGGTCGGCGCTCCCCTCGGCGGAGCCGCTGCCATTCCCCTCGAGGTCATCAAA$ $\tt CCTCAGCACAGGCTGTGTGGTCATCGTCGGCAGAATCGTCCTGTCCGGCAAACCCGCTTGCGAAAGCGCTGGCGTCCAGGAAGACGCTGCCTCCCTGA$ AGCCATGCCAGACCCAGATGGTTTTGGTTTTGCCTCCTGCTCAGCTCCAGCAGAGCGGAATCACAGGCGATAACACAACCACAAGCTCCGAGCCTGC GACCTCGAGGATAGGGATGAGGCTCAGCTCCACGTCTGGGTCCCCCCTCTGAATGTGAGAGGCGGAAGGGATGCCGTCATCCTCCTGATGTGCGTCGT GAAACGTCAGCGTCGCCCATGACGGAGCCGGAAAGAGAGTGTATTACCTCACCAGAGACCCCTACCACACCCCTCGCCAGAGCCGCTTGGGAAAGCGAA ${\tt CCCGCTCCCTGGGCTGTCCCCCTGACTCCGACGCTGAGTCCTACTCCAGCATGCCCCCTCTGGAAGGCGAACCCGGAGACCCTATCGGAGGCCATTA$ ATCTGCTCCCGCTATCCTCAGCCCTGGCGCTCTGGTCGTGGGAGTGGTCTGCGCTGCCATTCTGAGAATCCTCGACATGATCGCTGGCGCTCACTGG ${\tt GGGAAGCAGACCCTCCTGGGGACCCCTAGGAGAAGGTCCAGGAATTGGACAACCCAAGGCTGTAACTGTAGCATTTACCCTGGCCATATCA}$

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TCAGGGTCTGCGAAAAGATGATGGGATACATTCCCCTCGTGGGAGCCCCTCTGGGAGGCGCTGCCAGAGCCCTCGCCCATGGCGTCAGGGTCCTGGAA GACGGAGTGAATGGCGGAAACGCTGGCAGAACCACAAGCGGACTGGTCAGCCTCCTGACACCCGGAGCCAAACAGAATATCCAACTGATTAACACAAA CGGACTGGCTCTGCTCAGCTGTCTGACAGTGCCTGCCTCCGCCTATCAGGTCAGGAATAGCACAGGCCTCTACCATGTGACAAACGATTGCCCTGGCA $\tt CTGAGAAGGCATATCGATCTGCTCGGGAAGCGCTACCCTCTGCTCCGCCCTCTACGTCGGCGATCTGTGTGGCTCCCACGGCTCCCACAGGCTCCGG$ GGCCCCTCTACGGAAACGAAGGCTGTGGCTGGGCCGGATGGCTCCTGTCCCCCAGAGGCTCCACCGAAGACGTCGTGTGTTGCTCCATGTCCTACTCC ${\tt TTGGCGGAGCCGGAAACAATACCCTCCACTGTCCCACAAGCGTCGAGGAAGCCTGTAGCCTCACCCTCCCCATAGCGCTAAGTCCAAGTTTGGCTATAGCCGCTAGGCGCTAAGTCCAAGTTTGGCTATAGCCGCTAGGCGCTAAGTCCAAGTTTGGCTATAGCCGCTAGGCGCTAAGTCCAAGTTTGGCTATAGCCGCTAGGCGCTAAGTCCAAGTTTGGCTAAGTCAAGTCAAGTCAAGTTTGGCTAAGTCAAGTCAAGTCAAGTCAAGTCAAGTCAAGTTTGGCTAAGTCAAG$ $\tt CTGGCTCCGTGACAGTGCCTCACCCTAACATTGAGGAAGTGGCTCTGTCCACCACAGGCGAAATCCCTTTCTATGGCAAACTGGTCTTCGATATCACA$ AAGCTCCTGCTCGCCGTCTTCGGACCCCTCTGGATTCTGCAAGCCTCCCTGCTCAAGGTCCCCTATTTCGTCACCGCTGCCCTCGTGATGGCCCAACT $\tt CCCTGGATCCCACATTCACAATCGAAACCACAACCCTCCCCCAAGACGCTGTGTCCCACGGACCCACACCCCTCCTGTATAGGCTCGGCGCTGTGCAA$ AACGAAGTGACACTGACACCCTGTGACAAAGTATATCATGACCTGTGCCAGAGTGGCTATCAAAAGCCTCACCGAAAGGCTCTACGTCGGCGGACC AACACCCTGAGGCTACCTATAGCAGATGCGGAACCTGTGGCTCCAGCGATCTGTATCTGGTCACCAGACACGCTGACGTCATCCCTGTGAGAAGGAGA AGGCCTAGCTGGGGCCCTACCGATCCCAGAAGGAAGCAGAAACCTCGGCAAAGTGATTGACACATGCGGATTCGCTGACCTCGGCCCTGA ATCTGCCTTACATTGAGCAAGGCATGATGCTCGCCGAACAGTTTAAGCAAAAGGCTCTGGGACTGCTCCAGACATACCAAGCCACAGTGTGTGCCAGA ATAGCTCCGTGCTCTGCGAATGCTATGACGCTGGCTGTGCCTGGTACGACACCCGCTGAGACAACCGTCAGGCTCAGGGCTTACATGGGCTGG $\tt CTCCACCGCTCTGAATGCATTGCCTGAATACCGGATGGCTCGCCGGACTGTTTTACCAACACAAATTCAATAACGCTCTGTCCCAACTCCCTGC$ AGGAAAACCAAAAGGAATACCAATAGGAGACCCCAAGACGTCAAGTTTCCCGGAGGCCGGAAGCCAAACCAAACAGTCCGGCGAAAACTTTCCCTATCTACCGCTCTGGCTGACGCCACAAAGTCCTTCGGAAGCACAACCTCCAGGTCCGCCTGTCAGAGACAGAAAAAGGTCACCTTTGACAGACTGCAAGT GCTCGACTCCCACTATCAGGATGTGCTCGACCAAGCCGAAACCGCTGGCGCTAGGCTCGTGGTCCTGGCTACCCCTCCCGGAAGCGTCACCC ${\tt TCCCCCATCCCAATATCGAATTCCATTACGTCACCGGAATGACAACCGATAACCTCAAGTGTCCCTGTCAGGTCCCCTCCCCCGAATTCTTTACCGAATCCCCAATCCCAATCCCCAATCCCAATCCCAATCCCAATCCCAATCCCAATCCCAATCCCAATCCCAATCCCCAATCCCCAATCCCAATCCCAATCCCAATCCCAATCCCCAATCCCCAATCCCAATCCCAATCCCAATCCCAATCCCCAATCCCCAATCCCAATCCCAATCCCAATCCCAATCCCAATCCCAATCCCAATCCCAATCCCAATCCCCAATCCCAATCCCAATCCCAATCCCAATCCCAATCCCAATCCCAATCCCAATCCCAATCCCAATCCCAATCCCAATCCCAATCCCAATCCCAATCCCAATCCCAATCCCCCAATCCCAATCCCAATCCCAATCCCAATCCCAATCCCAATCCCAATCCCAATCCCAATCCCAATCCAATCCCAATCCAATCCAATCCCAATCCAATCCCAATCCAATCCAATCCAATCCAATCCAATCCCAATCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCCAATCAATCCAATCCAATCCAATCAA$ GAGCCTCCGGCGTCCTGACAACCTCCTGCGGAAACACACTGACATGCTATATCAAAGCCAGAGCCGCTTGCAGAGCCGCTGGCCTCTTCGATAGGCTC GGGAGAGAATTGCGGATACAGAAGGTGTAGGGGCTAGCGGAGTGCTCACCACAAGCTGTGGCAATACCCTCATCATGCACACAAGGTGTCACTGTGGCG $\tt CTGAGATTACCGGACACGTCAAGAATGGCACAATGAGAATCGTCGGCCCTAGGACATGCAGGAGGTCAGCTTTAGGGTCGGCCTCCACGAATACCCT$ GTGGGAAGCCAACTGCCTTGCGAACCCGAACCCGATGTGGCTGTGCTCACCTCCAAGGAAGTGAAAGCCGCTGCCTCCAAGGTCAAGGCTAACCTCCT $\tt CGTCGGCATTTTCAGAGCCGCTGACTTTGACCAAGGCTGGGGCCCTATCTCCTACGCTAACGGAAGCGGACCCGATCAGAGACCCTATTGCTGGCACT$ ${\tt ACCCATTGCCTCTGGATGATGCTCCTGATTAGCCAAGCCGAAGCCGCTCTGGAAAACCTCGTGATTCTGAATGCCGCTAGCCTCGCCGGAACCCCATAT$ $\tt CGTCTACCATGGCGCTGGCACAAGGACAATCGCTAGCCCTTGGGCTCACAATGGCCTCAGGGATCTGGCTGTGGGAACCCGTCGTGTTTAGCC$ AAATGGAAACCAAACTGATTACCTGGGGCGCTAAGGGACCCGTCATCCAAATGTATACCAATGTGGATCAGGATCTGGTCGGCTGGCCCGCTCCCCAA TCGAGCCTGTGTGTACCAGAGGCGTCGCCAAAGCCGTCGACTTTATCCCTGTGGAAAACCTCGAGACAACCATGAGGTCCCCCGTCTTCACAGACAAT GCCCTCGGCATTAACGCTGTGGCTTACTATAGGGGACTGGATGTGTCCGTGATTCCCACAAGCGGAGACGTCGTGGTCGTGGCTACCGATATGTCCGC

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 ${ t ATACCGGAGACTTTGACTCGTGATTGACTGTAACACATGCGTCACCCAAACCGTCGACTTTAGCCTCGACCCTAACACAAAACAGAAGGCCTCAGGAT$ ${\tt GGCCTCAGCGCTTTCTCCTGGACAGTGTATCACGGAGCCGGAACCAGAACCATTGCCTCCCCCAAAGGCCCTGTGATTCAGATGTACACAAACGTCGA$ ATAGGTCCGAGCTCAGCCCTCTGCTCCTGTCCACCACACAGTGGCAGGTCCTGCCTTGCCTCCTCACAACCCTCCCGGTCTGTCCACCGGACTGAGA AAGCTCGGCGTCCCCCTCTGAGAGCCTGGAGGCATAGGGCTAGGTCCGTGAGAGCCAGACTGCTCGCCAGAGGCGGAAGGGCTAGCCCTCTGACAAC TCCTGAAAGTGCCTTACTTTGTGAGAGTGCAAGGCCTCCTGAGAATCTGTGCCCTCGCCAGAAAGATGGTGAAAAACGGAACCATGAGGATTGTGGGA CCCAGAACCTGTAGGAATATGTGGAGCGGAACCTTTCCCATTAACGCTTACACAACCGGAGAGGTCGCCCTCAGCACAACCGGAGAGATTCCCTTTTA CGGAAAGGCTATCCCTCTGGAAGTGATTAAGGGAGGCAGACACCTCATCTTTCTGACAAGGGATCCCACAACCCCTĆTGGCTAGGGCTGCCTGGGAGA CAGCCAGACACACCCGTCAACTCCTGGCTCGGCAATATCATTAGGGTCAGCGCTGAGGAATACGTCGAGATTAGGAGAGTGGGAGACTTTCACTAT GAAAAGGACAGTGGTCCTGACAGAGTCCACCCTCAGCACAGCCCTCGCCGAACTGGCTACCAAAAGCTTTGGCTCCAGCTCCACCTCCGGCATTACCG GAGACAATACCACAACCTCCGTGTCCTGCCAAAGGGGATACAAAGGCGTCTGGAGAGGCGATGGCATTATGCATACCAGATGCCATTGCGGAGCCGAA CATTTCGTCGGCGCTGGCCTCGCCGGAGCCGCTATCGGAAGCGTCGGCCTCGGCAAAGTGCTCGTGGATATCCTCGCCGGATACGGAGCCGGAGACA GTGTATGAGGCTGCCGATGCCATTCTGCATACCCCTGGCTGTGTGCCTTGCGTCAGGGCAAGGCAATGCCTCCAGGTGTAGCTCCGGCTGTCCCGAAAG GTGACCTCGACCTCAGGCTAGGGTCGCCATTAAGTCCCTGACAGAGAGACTGTATGTGGGAGTGTCCAAGGGATGGAGACTGCTCGCCCCTATCACA GCCTATGCCCAACAGGCAACGGGACTGCTCGGCTGTATCATTACCTCCCTGACATTCTTTAGCGTCCTGATTGCCAGAGACCAACTGGAACAGGCTCT GGATTGCGAAATCTATGGCGCTTGCTATAGCATTGAGCCTCTGGATTGCCAAGTGCCTAGCCCTGAGTTTTTCACAGAGCTCGACGGAGTGAGACTGC ATAGGTTTGCCCCTGTAAGCCTCTGCTCAGGGAAACCTGTTACATTAAGGCTAGGGCTGCCTGTAGGGCTGCCGGACTGCAAGACTGTACCATG $\tt CTGGTCTGCGGAGACGATCTGGTCGTGATTATCGATCCCAATATCAGAACCGGAGTGAGAACCATTACCACAGGCTCCCCCATTACCTATAGCACATA$ $\tt CAACCCAATGGCAAACCGGACACAGAATGGCTTGGGATATGATGATGATTGGTCCCCACAGCCGCTCTGGTCATGGCTCAGCTCCTGAGAATCCCT$ CGATAGCCCTGACGCTGAGCTCATCGAAGCCAATCTGCTCTGGAGACAGGAAATGGGGAGGCAATATCACAAGGGTCGAGTCCGAGAATGAGGGAGTGT ${\tt TTACCGGACTGACACATTGACGCTCACTTTCTGTCCCAGACAAAGCAAAGCGGAGAATTTCCCTTACCTCGTGGCTAGGGGAAGGAGACAGCCT}$ ATCCCTAAGGCTAGGAGACCCGAAGGCAGAACCTGGGCCCAACCCGGATACCCTTGGCCTCTGTATGGCAATCTGATTGTGTTTTCCCGATCTGGGAGT GAGAGTGTGTGAGAAAATGGCTCTGTATGACGTCGTGTCCAAGCTCCCCCTCGCCGTCATGGGATACGCTACCGGAAACCTCCCCGGATGCTCCTTCT GGCGTCGCCGGAGCCCTCGTGGCTTTCAAAATCATGAGCGGAGAGGTCAGCTATAGCTCCATGCCTCCCCTCGAGGGAGAGCCTGGCGATCCCGATCT GTCCGACGGAAGCTGGAGCACAGTGTCCAGCGAAGCCGGAAGGCAAGAGATGGGCGGAAACATTACCAGAGTGGAAAAGCGAAAACAAAGTGGTCATCC $\tt TCGACTCCTTCGATCCCCTCGTGGCTGAGGAAGTGGGATGGCCTGCCCCTCAGGGAAGCCAGAAGCCTCACCCCTTGCACATGCGGAAGCTCCGACCTC$ TACCTCGTGACAAGGCATGCCGATGGCTGTAGCGGAGGCGCTTACGATATCATTATCTGTGACGAATGCCATAGCACAGACGCTACCTCCATCCTCGG $\tt CTGGCATTGACTGTTTCAGAAAGCATCCCGAAGCCACATACTCCAGGTGTGGCTCCGGCCCTTGGATTACCCCTAGGTGTCTGGTCGACTATCCCTAT$ $\tt CTGGCTGCCGGAGTGGGAATCTATCTGCTCCCCAATAGGGCTGCCGCCCTCGTGACACCCCTGTGCCGCTGAGGAACAGAAACTGCCTATCAATGCCCT$ TCTGTGAGGTCCTGTCCGACTTTAAGACATGGCTCAAGGCTAAGCTCATGCCTCAGCTCCCCGGAATCCCTTTCGTCAGCTGTCAGAGAGGGCTATAAG GGAGTGTGGAGGGGAGACGGAAGCCGGATCACACCCAGATGCCTCGTGGATTACCCTTTACAGACTGTGGCACTATCCCTGTACCATTAACTA TACCATTTTCAAA

HepC Savine Cassette Sequences (A+B+C) with specific restriction sites removed which can be joined to generate a single expressible open reading frame that encodes the hepc Savine protein above

Cassette A

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 $\tt CTGGGCTATCAAATGGGAATACGTCGTGCTCCTGTTTCTGCTCCTGGCTGACGCTAGGGTCTGCTCCCTGAATAACACAAA$ GGCCTCCCCTCGGCAATTGGTTTGGCTGTACCTGGATGAATAGCACAGGCTTTACCAAAGTGTGTGGCGCTCCCCCTTTC GTCGAGGGAGGGTCCAGATTGTGTCCAGCTCCCCCCTGCCGTCCCCCAAAGCTTTCAGGTCGCCCATCTGCATGCCCC ${\tt TACCGGAAGCGGAAAGTCCACCAAAGTGCCTGCCGCTAACACACCCCGGACTGCCTGTGTCAGGATCACCTCGAGTTTT}$ CACCAAATACATTATGACATGCATGAGCGCTGACCTCGAGGTCGTGACAAGCACATGGGTCCTGGTCGTGGGACTGATGG ATTTGCGGAAAGTATCTGTTTAACTGGGCCGTCAGGACAAAGCTCAAGCTCACCCCTATCGCTGCCGCTGGCAGACTGGA ATGGGTCCCCGGAGCCGTCTACGCTCTGTATGGCATGCAGCTCCCCTGTGAGCCTGAGCCTGACGTCGCCGTCCTGACAA GCATGCTGACAGACCCTAGCCATATCACAGCCGAAGCCGCTGGCAGAGACTCCGTGACACCCATTGACACAACCATTATG GCTAAGAATGAGGTCTTCTGTGTGCAACCCGAAAAGGGGAGGCAGAAAGCCTGCCAGATACGCTGCCCAAGGCTATAAGGT ${\tt CCTGGTCCTGAATCCCTCCGTGGCTGCCACACTGGGATTCGGAGCCTATATGTCCAAGGCTCACGGAGTGAGAAACTCCA}$ CCGGACTGTATCACGTCACCAATGACTGTCCCAATAGCTCCATCGTCTACGAAGCCGCTGACGCTATCCTCCACACAAGC TCCTACGGATTCCAATACTCCCCCGGACAGAGAGTGGAGTTtCTCGTGCAAGCCTGGAAGTCCAAGAAAACCCCTATGGG GCCCTGCCGATGGCATGAGCCAACTGTCCGCCCCTAGCCTCAAGGCTACCTGTACCGCTAACCATGACTCCCCCGATGCC CACCACAAGCCAAACCCTCCTGTTTAACATTCTGGGACTGGTCCAGGCTTGGAAAAGCAAAAAGACACCCATGGGCTTTA $\tt CTCAGGAAAAGCAGAAGGTTTGCCCAAGCCCTCCCCGTCTGGGCTAGGCCTGACTATATGTTTGCCCCTACCCTCTGGGC$ TAGGATGATCCTCATGACACACTTTTTCTCCGTGCTCATCGCTAGGGATCAGCTCGAGCAAGCCCTCAGCGTCATCCCTA ALGTCCAGTATCTGTATAAGGGAAGGTGGGTGCCTGGCGCTGTGTATGCCCTCTACGGAATGTGGCCCCTCCTGCTCCTG $\tt CTCCTGGCTCTGGCTCAGAGAGCCTATAGCCCTATCACATACTCCACCTATGGCAAATTCCTCGCCGATGGCGGATGCTC$ CGGCGGAGCCTATGACATTATCATTTGCGATGAGTGTGCCAGAAGCGTCAGGGCTAGGCTCCTGGCTAGGGGAGGCAGAG GATCTGCTCGAGGATAGCGTCACCCCTATCGATACCACAATCATGGCCAAAAACGAGTTLACACCCTCCCCGTCGTGGT CGGCACAACCGATAGGTCCGGCGCTCCCACATACTCCTGGGGAGCCAATGACACAGACGTCTTCGTCCCCGGATGCGTCC CCTGTGTGAGAGAGGGAAACGCTAGCAGATGCTGGGTGGCTATGACACCCACAGTGGCTACCAGAGACGGAAAGCTCCAG GATTGCACAATGCTCGTGTGTGGCGATGACCTCGTGGTCATCTGTGAGTCCGCCGGAGTGCAAGAGGATGCCGCTAGCCT ${\tt CAGGGCTGTGGCTGTGGTCGCCTTTAAGATTATGTCCGGCGAAGTGCCTAGCACAGAGGATCTGGTCAACCTCC}$ TGCCTGCCATTCTGTCCTACGATACCAGATGCTTTGACTCCACCGTCACCGAAAGCGATATCAGAACCGAAGAGGCTATC TATCAGTGTTGCGATCTcGAcCCCCAAGAGCTCACCCCTGCCGAAACCACAGTGAGACTGAGAGCCTATATGAATACCCC TGGCCTCCCCGTCTGCCAAGACCATCTGGAgTTtTGGCCCCAACCCGAATACGATCTGGAACTGATTACCTCCTGCTCCA GCAATGTGTCCGTGGCTCACGATGGCGCTGGCAAAAGGGTCTACTATCTGGGAAAGGTCATCGATACCCTCACCTGTGGC AGGCGGAAGGCATCTGATTTTCTGTCACTCCAAGAAAAAGTGTGACGAACTGGCTGCCAAACTGGTCGGCGGAGTGCTCG GAAAGCGCTGGCGTCCAGGAAGACGCTGCCTCCCTGAGAGCCTTTACCGAAGCCATGACCAGATACTCCGCCCCTCCCGG AGACCCTGGCTGGTTCACAGCCGGATACTCCGGCGGAGACATTTACCATAGCGTCAGCCATGCCAGACCCAGATGGTTTT GGTTTTGCCTCCTGCTCAGCTCCAGCACAAGCGGAATCACAGGCGATAACACAACCACAAGCTCCGAGCCTGCCCCTAGC GGATGCCCTCCCGATAGCGATGCCGAAAGGACACAGAGAAGGGGAAGGACAGGCAGAGCCAGAACCCGGAATCTATAGGTT AATGTGAGAGGCGGAAGGGATGCCGTCATCCTGATGTGCGTCGTGCATCCCACACTGGGAGTGAGAGCCACAAGGAA AACCTCCGAGAGACCCAGAGGCAGAAGGCAACCCATTCCCAAAGCCAGAAGGCCTGAGGGAAACGTCAGCGTCG ${\tt CCCATGACGGAGCCGGAAAGAGAGTGTATTACCTCACCAGAGACCCTACCACACCCCTCGCCAGAGCCGCTTGGGAAAGC}$ GAACCCGCTCCCTCCGGCTGTCCCCCTGACTCCGACGCTGAGTCCTACTCCAGCATGCCCCCTCTGGAAGGCGAACCCGG GCAGACCCTCCTGGGGACCCACAGACCCTAGGAGAAGGTCCAGGAATgtcgactgagaattcgcc

Cassette B

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GCTGGCAGAACCACAAGCGGACTGGTCAGCCTCCTGACACCCGGAGCCAAACAGAATATCCAACTGATTAACACAAACGG ${\tt ACTGGCTCTGCTCAGCTGTCTGACAGTGCCTCCGCCTATCAGGTCAGGAATAGCACAGGCCTCTACCATGTGACAA}$ ${\tt ACGATTGCCCTGGCAGAGACAAAAACCAAGTGGAAGGCGAAGTGCAAATCGTCAGCACAGCCGCTCAGACATTCCTCGCC}$ CGCCCTCTACGTCGGCGATCTGTGTGGCTCCCACGCTCCCACAGGCTCCGGCAAAAGCACAAAGGTCCCCGCTGCCTATG GGAAACGAAGGCTGTGGCTGGGCCGGATGGCTCCTGTCCCCCAGAGGCTCCACCGAAGACGTCGTGTTGCTCCATGTC $\tt CCGCTAGCTGTGGCGGAGTGGTCCTGGTCGGCCTCATGGCTCTGACACTGTCCCCCTATTACAAAAGGTATTGGATGAAC$ TCCACCGGATTCACAAAGGTCTGCGGAGCCCCTCCCTGTGTGATTGGCGGAGCCGGAAACAATACCCTCCACTGTCCCAC AAGCGTCGAGGAAGCCTGTAGCCTCACCCCTCCCCATAGCGCTAAGTCCAAGTTTGGCCTATGGCGCTAAGGATGTGAGAT GCCATGCCAGAATCTCCGGCATTCAGTATCTGGCTGGCCTCAGCACACTGCCTGGCAATCCCGCTATCGCTAGCCTCATG GCTTTCACAGCCGCTGTGACACAGATTGTGGGAGGCGTCTACCTCCTGCCTAGGAGAGGCCCTAGGCTCGGCGTCAGGGC ATTATCATGTTCGCTCCCACACTGTGGGCCAGAATGATTCTGATGACCCATGAGAATCTGGAAACCACAATGAGAAGCCC TGACAGTGCCTCACCCTAACATTGAGGAAGTGGCTCTGTCCACCACAGGCGAAATCCCTTTCTATGGCAAACTGGTCTTC ${\tt GATATCACAAAGCTCCTGCTCGCCGTCTTCGGACCCCTCTGGATTCTGCAAGCCTCCTGCTCAAGGTCCCCTATTTCGTCAAGGTCCCTATTTCGTCAAGGTCCCCTATTTCGTCAAGGTCCCCTATTTCGTCAAGGTCCCCTATTTCGTCAAGGTCCCCTATTTCGTCAAGGTCCCCTATTTCGTCAAGGTCCCCTATTTCGTCAAGGTCCCCTATTTCGTCAAGGTCCCCTATTTCGTCAAGGTCCCCTATTTCGTCAAGGTCCCCTATTTCGTCAAGGTCCCCTATTTCGTCAAGGTCCCCTATTTCGTCAAGGTCCCCTATTTCGTCAAGGTCCCCTATTTCGTCAAGGTCCCCTATTTCGTCAAGGTCCCCTATTTCGTCAAGGTCCCCTATTTCAAGGTCAAGGTCCCCTATTTCAAGGTCCCCTATTTCAAGGTCCCCTATTTCAAGGTCCCCTATTTCAAGGTCCCCTATTTCAAGGTCCCCTATTTCAAGGTCCCCTAATTTCAAGGTCCCCTATTTCAAGGTCCCCTATTTCAAGGTCCCCTAATTTCAAGGTCCCCTAAGGTCAAGGTCCCCTAATTTCAAGGTCCCCTAATTTCAAGGTCCCCTAATTTCAAGGTCCCCTAAGGTCAAGGTCCCCTAATTTCAAGGTCAAGGTCCCCTAAGGTCAAG$ CACCGCTGCCCTCGTGATGGCCCAACTGCTCAGGATTCCCCAAGCCATTCTGGATATGATTGCCGGAGCCCATTGGGGAG ACACCCTGTGACAAAGTATATCATGACCTGTGCCAGAGTGGCTATCAAAAGCCTCACCGAAAGGCTCTACGTCGGCGGAC ${\tt CCTACCGATTGCTTTAGGAAACACCCTGAGGCTACCTATAGCAGATGCGGAACCTGTGGCTCCAGCGATCTGTATCTGTATCTGGTATCTGTATCTGTATCTGGTATCTGGTATCTGGTATCTGGTATCTGGTATCTGGTATCTGGTATCT$ GATGCCACAAGCATTCTGGGAATCGGAACCGTCCTGGATCAGGCTGAGACAGCCGGAGCCAGACTGGTCGTCGCCAC ATACGTCCCGAAAGCGATGCCGCTGCCAGAGTGACAGCCATTCTGTCCAGCCTCACCGTCACCCAACTGCTCAGGAGAC TGCATCAGTGGAGGCCTAGCTGGGGCCCTACCGATCCCAGAAGGAGAAAGCAGAAACCTCGGCAAAGTGATTGACACACTG ACATGCGGATTCGCTGACCTCGGCCCTGACCAAAGGCCTTACTGTTGGCATTACCCTCCCAAACCCTGTGGCATTGTGCC $\tt CCGAACAGTTTAAGCAAAAGGCTCTGGGACTGCTCCAGACATACCAAGCCACAGTGTGTGCCAGAGCCCAAGCCCCTCCC$ ${\tt GATGGCTCCTGGTCCACCGTCAGCTCCGAGGCTGGCACAGAGGATGTGGTCTGCTGTAGCATGAGCTATAGCTGGACCGG}$ $\tt CCGTCCAGAATCTGGCTGAGCAATTCAAACAGAAAGCCCTCGGCCTCCTGCAAACCGCTAGCAGACAGGCTGAGGTCATC$ GCTCCCGCTGTGCAAACCAATTGGCAAAAGCTCGAGGTCTTCTGGGCCAAACACATGTGGAATTCATTAGCGGAATCCA ATACCTCGCCGGACTGTCCACCCTCCCCGGACTGATTGCCTTTGCCTCCAGGGGAAACCATGTGTCCCCCACACACTATG GGAAGCGTCTTCCTCGTGGGACAGCTCTTCACATTCTCCCCCAGAAGGCATAGCTCCGTGCTCTGCGAATGCTATGACGC TGGCTGTGCCTGGTACGAACTGACACCCGCTGAGACAACCGTCAGGCTCAGGGCTTACATGGGCTGGGTGGCTGCCCAAC ATTAACTCCACCGCTCTGAATTGCAATGAGTCCCTGAATACCGGATGGCTCGCCGGACTGTTTTACCAACACAACATATACAA TAACGCTCTGTCCAACTCCCTGCTCAGGCATCACAATCTGGTCTACTCCACCACCAAGCAGAAGCGCTTGCCAAAGGCAAA AGAAAGTGACAGCCGCTATGTCCACCAATCCCAAACCCCAAAGGAAAACCAAAAGGAATACCAATAGGAGACCCCAAGAC GTCAAGTTTCCCGGAGGCGGAAGCCAAACCAAACAGTCCGGCGAAAACTTTCCCTATCTGGTCGCCTATCAGGCTACCGT ACAATACCAGACCCCTCTGGGAAACTGGTTCGGATGCACAGTGCCTCCCCCTAGGAAAAAGAGAACCGTCGTGCTCACC GAAAGCACACTGTCCACCGCTCTGGCTGAGCTCGCCACAAAGTCCTTCGGAAGCACAACCTCCAGGTCCGCCTGTCAGAG ACAGAAAAAGGTCACCTTTGACAGACTGCAAGTGCTCGACTCCACTATCAGGATGTGCTCGACCAAGCCGAAACCGCTG GCGCTAGGCTCGTGGTCCTGGCTACCGCTACCCTCCCGGAAGCGTCACCGTCCCCATCCCAATATCGAGTTtCATTAC $\tt CCTGAAACTGACACCCATTGCCGCTGCCGGAAGGCTCGACCTCAGCGGATGGTTTACCGCTGGCTATAGCGGAGGCGATA$ ${\tt GCTAAGCATATGTGGAACTTTTGCAGAGGCCTCCGGCGTCCTGACAACCTCCTGCGGAAACACACTGACATGCTATATCAA}$ AGCCAGAGCCGCTTGCAGAGCCGCTGGCCTCTTCGATAGGCTCCAGGTCCTGGATAGCCATTACCAAGACGTCCTGAAAG AGGTCAAGGCTGCCGCTAGCAAAGTGAAAGCCAATCTGCTCGGCCCTCTGACAAACTCCAGGGGAGAATTGCGGATAC AGAAGGTGTAGGGCTAGCGGAGTGCTCACCACAAGCTGTGGCAATACCCTCATCATGCACACAAGGTGTCACTGTGGCGC TGAGATTACCGGACACGTCAAGAATGGCACAATGAGAATCGTCGGCCCTAGGACATGCAGAGAGGGTCAGCTTTAGGGTCG GCCTCCACGAATACCCTGTGGGAAGCCAACTGCCTTGCGAACCCGAACCCGATGTGGCTGTGCTCACCTCCAAGGAAGTG AAAGCCGCTGCCCAAGGTCAAGGCTAACCTCCTGTCCGGAAGAGGCTTGCTCCCTGACACCCCCTCACTCCGCCAA AGGCAGAGACGCTGTGATTCTGCTCATGTGTGTGGTCCACCCTACCCTCGTGTTTGACATTACCAAACTGCTCCTGGCTG AATAGGCTCATCGCTTCGCTAGCAGAGGCAATCACGTCAGCCCTACCCATctcgagtgagaattcgcc

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Cassette C

TCTGAATGCCGCTAGCCTCGCCGGAACCCATATCATTCCCGATAGGGAAGTGCTCTACAGAGAGTTTGACGAAATGGAAG GCGCTTACATGAGCAAAGCCCATGGCATTGACCCTAACATTAGGACAGGCGTCAGGACAATCACAACCGGAAGGGTCCAG GGACTGCTCAGGATTTGCGCTCTGGCTAGGAAAATGATTGGCGGACACTATGTGCAAATGGCTATCATTAAGCTCGGCGC TAGGAGATTCGCTCAGGCTCTGCCTGTGTGGGCCAGACCCGATTACAATCCCCCTCTGGTCGAGACATGGAAAAAGCCTG ACTATGAGCCTACCGCTGCCCAAACCTTTCTGGCTACCTGTATCAATGGCGTCTGCTGGACCGTCTACCATGGCGCTGGC ACAAGGACAATCGCTAGCCCTTGGGCTCACAATGGCCTCAGGGATCTGGCTGTGGCTGTGGAACCCGTCGTGTTTAGCCA AATGGAAACCAAACTGATTACCTGGGGCGCTAAGGGACCCGTCATCCAAATGTATACCAATGTGGATCAGGATCTGGTCG GCTGGCCCGCTCCCCAAGGCTCCAGGTCCCTGACACCCTGTAAGGTCGTGATTCTGGATAGCTTTGACCCTCTGGTCGCC GAAGAGGATGAGAGAGAGATTAGCGTCCCCGCTGAGATTCTGAGAAAGTCCCTGACAGGCACATACGTCTACAATCACCT CACCCCTCTGAGAGACTGGGCCCATAACGGACTGAGAGACCTCGCCGTCGCCGTCGAGCCTGTGTGTACCAGAGGCGTCG ATTAACGCTGTGGCTTACTATAGGGGACTGGATGTCCCGTGATTCCCACAAGCGGAGACGTCGTGGTCGTGGCTACCGA GTgGA\tTTTAGCCTCGACCCTAACACAAACAGAAGGCCTCAGGATGTGAAATTCCCTGGCGGAGGCCCAAATCGTCGGCGG AGTGTATCTGCTCCCCAGAAGGGGACCCAGAAGGGCTCTGGCTCACGGAGTGAGAGTGCTCGAGGATGGCGTCAACTATG GCTAGGAAAGCCGTCGCCCATATCAATAGCGTCTGGAAAGACCTCCTGGAAACCCTTGGCGCTAAGCAAAACATTCAGCT GCCTCTTCTATCAGCATAAGTTTAACTCCAGCGGATGCCCTGAGAGACTGGCTAGCTGTAGGAGACTGACAGTGGTCCTG CGACTGTGAGATTTACGGAGCCTGTTACTCCATCGAACCCCTCGACCTCCCCCCTATCATTCAGAGACTGCATGGCCTCA GCGCTTTCTCCTGGACAGTGTATCACGGAGCCGGAACCAGAACCATTGCCTCCCCAAAGGCCCTGTGATTCAGATGTAC ACAAACGTgGA+CAAGACCTCTACAGATTCGTCGCCCCTGGCGAAAGGCCTAGCGGAATGTTTGACTCCAGCGTCCTGTG TGAGTGTTÄCGATGCCGGATGCGCTTGGTATAGGTCCGAGCTCAGCCCTCTGCTCCTGTCCACCACACAGTGGCAGGTCC TGCCTTGCTCCTTCACAACCCTCCCGCTCTGTCCACCGGACTGAGAAAGCTCGGCGTCCCCCCTCTGAGAGCCTGGAGG CTTCAATATCCTCGGCGGATGGGTCGCCGCTCAGCTCGCCGCTCCCGGAGCCGCTACCGCTCTGTGGATtCTCCAGGCTA GCCTCCTGAAAGTGCCTTACTTTGTGAGAGTGCAAGGCCTCCTGAGAATCTGTGCCCTCGCCAGAAAGATGGTGAAAAAC GGAACCATGAGGATTGTGGGACCCAGAACCTGTAGGAATATGTGGAGCGGAACCTTTCCCATTAACGCTTACACAACCGG AGAGGTCGCCCTCAGCACAACCGGAGAGATTCCCTTTTACGGAAAGGCTATCCCTCTGGAAGTGATTAAGGGAGGCAGAC TGTTTACCTTTAGCCCTAGGAGACACTGGACCACACAGGGATGCAATTGCTCCATCTATCCCGGACACATTTTCGTCGGC GCTGGCCTGGCGGAGCCGCTATCGGAAGCGTCGGCCTCGGCAAAGTGCTCGTGGATATCCTCGCCGGATACGGAGCCGG AGACATTTGGGATTTGCGAAGTGCTCAGCGATTTCAAAACCTGGCTGAAAGCCAAACTGATGCCCCAACTGCCTG GAAGGCAATGCCTCCAGGTGTAGCTCCGGCTGTCCCGAAAGGCTCGCCTCCTGCAGAAGGCTCACCGATTTCGATCAGGG GGGTCGCCATTAAGTCCCTGACAGAGAGACTGTATGTGGGAGTGTCCAAGGGATGGAGACTGCTCGCCCCTATCACAGCC TATGCCCAACAGACAAGGGGACTGCTCGGCTGTATCATTACCTCCCTGACATTCTTTAGCGTCCTGATTGCCAGAGACCA ${\tt ACTGGAACAGGCTCTGGATTGCGAAATCTATGGCGCTTGCTATAGCATTGAGCCTCTGGATTGCCAAGTGCCTAGCCCTG}$ ATTAAGGCTAGGGCTGCCTGTAGGGCTGCCGGACTGCAAGACTGTACCATGCTGGTCTGCGGAGACGATCTGGTCGTGAT TATCGATCCCAATATCAGAACCGGAGTGAGAACCATTACCACAGGCTCCCCCATTACCTATAGCACATACGGAAAGTTTC $\tt TGGCTGACGGATGCAATTGGACAAGGGGAGAGAGAGATGCGATCTGGAAGACAGAAGCGAACTGTCCCCCTCCTG$ CTCAGCACAACCCAATGGCAAACCGGACACAGAATGGCTTGGGATATGATGATGATTGGTCCCCCACAGCCGCTCTGGT ACGTCGGCCCTGGCGAAGGCGCTGTGCAATGGATGAACAGACACGATAGCCCTGACGCTGAGCTCATCGAAGCCAATCTG CTCTGGAGACAGGAAATGGGAGCCAATATCACAAGGGTCGAGTCCGAGAATGAGGGAGTGTTTACCGGACTGACACAC TGACGCTCACTTTCTGTCCCAGACAAAGCAAAGCGGAGAGATTTCCCTTACCTCGTGGCTAGGGGAAGGAGACAGCCTA TCCCTAAGGCTAGGAGACCCGAAGCCTGGGCCCAACCCGGATACCCTTGGCCTCTGTATGGCAATCTGATTGTG ATACGCTACCGGAAACCTCCCGGGATGCTCCTTCTCCATCTTTCTGCTCGCCTCCTGTCCTGCCTCACCGTCCCGCTA $\tt GCGCTTACCAACTGGGAAAGGTCCTGGT\mathring{g}GALATTCTGGCTGGCTATGGCGTGGCGTCGCCGGAGCCCTCGTGGCTTTC$ AAAATCATGAGCGGAGAGGTCAGCTATAGCTCCATGCCTCCCCTCGAGGGAGAGCCTGGCGATCCCGATCTGTCCGACGG AAGCTGGAGCACAGTGTCCAGCGAAGCCGGAAGCCAAGAGATGGGCGGAAACATTACCAGAGTGGAAAGCGAAAACAAAG $\tt CCTTGCACATGCGGAAGCTCCGACCTCTACCTCGTGACAAGGCATGCCGATGGCTGTAGCGGAGGCGCTTACGATATCAT$ ${\tt TATCTGTGACGAATGCCATAGCACAGACGCTACCTCCATCCTCGGCATTGGCACAGTGCTCACCTTTACCATTGAGACAA}$ $\tt CCACACTGCCTCAGGATGCCGTCAGCAGAACCCAAAGGAGAGGCAGAACCGGAAAGGCGAAAGCCTTGGCATTGACTGTTTC$ AGAAAGCATCCCGAAGCCACATACTCCAGGTGTGGCTCCGGCCCTTGGATTACCCCTAGGTGTCTGGTgGALTATCCCTA ${\tt TCTGGCTGCCGGAGTGGGAATCTATCTGCTCCCCAATAGGGCTGCCGCCCTCGTGACACCCTGTGCCGCTGAGGAACAGA}$

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AACTGCCTATCAATGCCCTCAGCAATAGCCTCCTGAGACACCCTTACCTCGTGTATATCTCCAGCGAATGCACAACCCCTTGCTCCGGCTCCTGGCTCCAGGCAATGCACAACCCCTTGCTCCGGCTCCTGGCTCAGGGATATCTGGGACTGGATCTGAGGCTAAGCTTTAAGACATGGCTCAAGGCTAAGCCTCATGCCTCAGCTCCCCGGAATCCCTTTCGTCAGCTGTCAGAGAGGGCTATAAGGAGTGTGGAGGGGAGACCGAACCCTGGATCACAGACTGTGACCATTAACCATTACCATTTCCAAAAagatctTGAgtcgacgaattcgcc

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Melanoma Savine design

Two savines - one containing scrambled melanocyte differentiation Ags
- one containing scrambled melanoma cancer specific Ags

Genes in melanocyte differentiation Savine

ap100

MDLVLKRCLLHLAVIGALLAVGATKVPRNQDWLGVSRQLRTKAWNRQLYPEWTEAQRLDCWRGGQVSLKVSNDGPTLI GANASFSIALNFPGSQKVLPDGQVIWVNNTIINGSQVWGGQPVYPQETDDACIFPDGGPCPSGSWSQKRSFVYVWKTW GQYWQVLGGPVSGLSIGTGRAMLGTHTMEVTVYHRRGSRSYVPLAHSSSAFTITDQVPFSVSVSQLRALDGGNKHFLR NQPLTFALQLHDPSGYLAEADLSYTWDFGDSSGTLISRALVVTHTYLEPGPVTAQVVLQAAIPLTSCGSSPVPGTTDG HRPTAEAPNTTAGQVPTTEVVGTTPGQAPTAEPSGTTSVQVPTTEVISTAPVQMPTAESTGMTPEKVPVSEVMGTTLA EMSTPEATGMTPAEVSIVVLSGTTAAQVTTTEWVETTARELPIPEPEGPDASSIMSTESITGSLGPLLDGTATLRLVK RQVPLDCVLYRYGSFSVTLDIVQGIESAEILQAVPSGEGDAFELTVSCQGGLPKEACMEISSPGCQPPAQRLCQPVLP SPACQLVLHQILKGGSGTYCLNVSLADTNSLAVVSTQLIMPGQEAGLGQVPLIVGILLVLMAVVLASLIYRRRLMKQD FSVPQLPHSSSHWLRLPRIFCSCPIGENSPLLSGQQV

MART

MPREDAHFIYGYPKKGHGHSYTTAEEAAGIGILTVILGVLLLIGCWYCRRRNGYRALMDKSLHVGTQCALTRRCPQEG FDHRDSKVSLQEKNCEPVVPNAPPAYEKLSAEQSPPPYSP

TRP-1

PAFLTWHRYHLLRLEKDMQEMLQEPSFSLPYWNFATGKNVCDICTDDLMGSRSNFDSTLISPNSVFSQWRVVCDSLED YDTLGTLCNSTEDGPIRRNPAGNVARPMVQRLPEPQDVAQCLEVGLFDTPPFYSNSTNSFRNTVEGYSDPTGKYDPAV RSLHNLAHLFLNGTGGQTHLSSQDPIFVLLHTFTDAVFDEWLRRYNADISTFPLENAPIGHNRQYNMVPFWPPVTNTE MFVTAPDNLGYTYE

Tyros

MLLAVLYCLLWSFQTSAGHFPRACVSSKNLMEKECCPPWSGDRSPCGQLSGRGSCQNILLSNAPLGPQFPFTGVDDRE SWPSVFYNRTCQCSGNFMGFNCGNCKFGFWGPNCTERRLLVRRNIFDLSAPEKDKFFAYLTLAKHTISSDYVIPIGTY GQMKNGSTPMFNDINIYDLFVWMHYYVSMDALLGGSEIWRDIDFAHEAPAFLPWHRLFLLRWEQEIQKLTGDENFTIP YWDWRDAEKCDICTDEYMGGQHPTNPNLLSPASFFSSWQIVCSRLEEYNSHQSLCNGTPEGPLRRNPGNHDKSRTPRL PSSADVEFCLSLTQYESGSMDKAANFSFRNTLEGFASPLTGIADASQSSMHNALHIYMNGTMSQVQGSANDPIFLLHH AFVDSIFEQWLQRHRPLQEVYPEANAPIGHNRESYMVPFIPLYRNGDFFISSKDLGYDYSYLQDSDPDSFQDYIKSYL EQASRIWSWLLGAAMVGAVLTALLAGLVSLLCRHKRKQLPEEKQPLLMEKEDYHSLYQSHL

בם את

MSPLWWGFLLSCLGCKILPGAQGQFPRVCMTVDSLVNKECCPRLGAESANVCGSQQGRGQCTEVRADTRPWSGPYILR NQDDRELWPRKFFHRTCKCTGNFAGYNCGDCKFGWTGPNCERKKPPVIRQNIHSLSPQEREQFLGALDLAKKRVHPDY VITTQHWLGLLGPNGTQPQFANCSVYDFFVWLHYYSVRDTLLGPGRPYRAIDFSHQGPAFVTWHRYHLLCLERDLQRL IGNESFALPYWNFATGRNECDVCTDQLFGAARPDDPTLISRNSRFSSWETVCDSLDDYNHLVTLCNGTYEGLLRRNQM GRNSMKLPTLKDIRDCLSLQKFDNPPFFQNSTFSFRNALEGFDKADGTLDSQVMSLHNLVHSFLNGTNALPHSAANDP IFVVLHSFTDAIFDEWMKRFNPPADAWPQELAPIGHNRMYNMVPFFPPVTNEELFLTSDQLGYSYAIDLPVSVEETPG WPTTLLVVMGTLVALVGLFVLLAFLQYRRLRKGYTPLMETHLSSKRYTEEA

MC1R

MAVQGSQRRLLGSLNSTPTAIPQLGLAANQTGARCLEVSISDGLFLSLGLVSLVENALVVATIAKNRNLHSPMYCFIC CLALSDLLVSGTNVLETAVILLLEAGALVARAAVLQQLDNVIDVITCSSMLSSLCFLGAIAVDRYISIFYALRYHSIV TLPRAPRAVAAIWVASVVFSTLFIAYYDHVAVLLCLVVFFLAMLVLMAVLYVHMLARACQHAQGIARLHKRQRPVHQG FGLKGAVTLTILLGIFFLCWGPFFLHLTLIVLCPEHPTCGCIFKNFNLFLALIICNAIIDPLIYAFHSQELRRTLKEV LTCSW

MUC1F

 ${\tt MTPGTQSPFFLLLLTVLTVVTGSGHASSTPGGEKETSATQRSSVPSSTEKNAVSMTSSVLSSHSPGSGSSTTQGQDVTLAPATEPASGSAATWGQDVTSVPVTRPALGSTTPPAHDVTSAPDNK}$

Figure 27

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MUC1R

NRPALGSTAPPVHNVTSASGSASGSASTLVHNGTSARATTTPASKSTPFSIPSHHSDTPTTLASHSTKTDASSTHHSS VPPLTSSNHSTSPQLSTGVSFFFLSFHISNLQFNSSLEDPSTDYYQELQRDISEMFLQIYKQGGFLGLSNIKFRPGSV VVQLTLAFREGTINVHDVETQFNQYKTEAASRYNLTISDVSVSDVPFPFSAQSGAGVPGWGIALLVLVCVLVALAIVY LIALAVCQCRRKNYGQLDIFPARDTYHPMSEYPTYHTHGRYVPPSSTDRSPYEKVSAGNGGSSLSYTNPAVAAASANL

NB Muc 1 Repeat sequences in the middle of the gene were removed

Genes in melanoma specific Savine

BAGE

MAARAVFLALSAQLLQARLMKEESPVVSWRLEPEDGTALCFIF

GAGE - :

MSWRGRSTYRPRPRRYVEPPEMIGPMRPEQFSDEVEPATPEEGEPATQRQDPAAAQEGEDEGASAGQGPKPEADSQEQ GHPQTGCECEDGPDGQEMDPPNPEEVKTPEEEMRSHYVAQTGILWLLMNNCFLNLSPRKP

gp100In4

SWSQKRSFVYVWKTWGEGLPSQPIIHTCVYFFLPDHLSFGRPFHLNFCDFL

MAGE-1

MSLEQRSLHCKPEEALEAQQEALGLVCVQAATSSSSPLVLGTLEEVPTAGSTDPPQSPQGASAFPTTINFTRQRQPSE GSSSREEEGPSTSCILESLFRAVITKKVADLVGFLLLKYRAREPVTKAEMLESVIKNYKHCFPEIFGKASESLQLVFG IDVKEADPTGHSYVLVTCLGLSYDGLLGDNQIMPKTGFLIIVLVMIAMEGGHAPEEEIWEELSVMEVYDGREHSAYGE PRKLLTQDLVQEKYLEYRQVPDSDPARYEFLWGPRALAETSYVKVLEYVIKVSARVRFFFPSLREAALREEEEGV

MAGE-3

MPLEQRSQHCKPEEGLEARGEALGLVGAQAPATEEQEAASSSSTLVEVTLGEVPAAESPDPPQSPQGASSLPTTMNYPLWSQSYEDSSNQEEEGPSTFPDLESEFQAALSRKVAELVHFLLLKYRAREPVTKAEMLGSVVGNWQYFFPVIFSKASSSLQLVFGIELMEVDPIGHLYIFATCLGLSYDGLLGDNQIMPKAGLLIIVLAIIAREGDCAPEEKIWEELSVLEVFEGREDSILGDPKKLLTQHFVQENYLEYRQVPGSDPACYEFLWGPRALVETSYVKVLHHMVKISGGPHISYPPLHEWVLREGEE

PRAME

MERRLWGSIQSRYISMSVWTSPRRLVELAGQSLLKDEALAIAALELLPRELFPPLFMAAFDGRHSQTLKAMVQAWPF TCLPLGVLMKGQHLHLETFKAVLDGLDVLLAQEVRPRRWKLQVLDLRKNSHQDFWTVWSGNRASLYSFPEPEAAQPMT KKRKVDGLSTEAEQPFIPVEVLVDLFLKEGACDELFSYLIEKVKRKKNVLRLCCKKLKIFAMPMQDIKMILKMVQLDS IEDLEVTCTWKLPTLAKFSPYLGQMINLRRLLLSHIHASSYISPEKEEQYIAQFTSQFLSLQCLQALYVDSLFFLRGR LDQLLRHVMNPLETLSITNCRLSEGDVMHLSQSPSVSQLSVLSLSGVMLTDVSPEPLQALLERASATLQDLVFDECGI TDDQLLALLPSLSHCSQLTTLSFYGNSISISALQSLLQHLIGLSNLTHVLYPVPLESYEDIHGTLHLERLAYLHARLR ELLCELGRPSMVWLSANPCPHCGDRTFYDPEPILCPCFMPN

TRP2IN2

LMETHLSSKRYTEEAGGFFPWLKVYYYRFVIGLRVWQWEVISCKLIKRATTRQP

NYNSO1a

 ${\tt MQAEGRGTGGSTGDADGPGGPGIPDGPGGNAGGPGEAGATGGRGPRGAGAARASGPGGGAPRGPHGGAASGLNGCCRCGARGPESRLLEFYLAMPFATPMEAELARRSLAQDAPPLPVPGVLLKEFTVSGNILTIRLTAADHRQLQLSISSCLQQLSLMWITQCFLPVFLAQPPSGQRR$

NYNSO1b

 ${\tt MLMAQEALAFLMAQGAMLAAQERRVPRAAEVPGAQGQQGPRGREEAPRGVRMAARLQG}$

LAGE1

Differentiation Savine Scramble process

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 ${\tt MQAEGQGTGGSTGDADGPGGPGIPDGPGGNAGGPGEAGATGGRGPRGAGARASGPRGGAPRGPHGGAASAQDGRCPCGARRPDSRLLQLHITMPFSSPMEAELVRRILSRDAAPLPRPGAVLKDFTVSGNLLFIRLTAADHRQLQLSISSCLQQLSLLMWITQCFLPVFLAQAPSGQRR$

```
Disease name
               : melanoma
Input filename : Diffmucg.txt
Output filename : Diffmucs.txt
Number genes
              : 8
Number segments : 187
Segment length : 30
Segment overlap : 15
Segments in original order:
Gene
        : gp100
Segment#
        : 1
Offset
        : 1
1st Codon : 1
 A A M D L V L K R C L L H L A V I G A L L A V G A T K V P R
Gene
         : gp100
Segment#
Offset
        : 16
1st Codon: 1
V I G A L L A V G A T K V P R N Q D W L G V S R Q L R T K A
GTGATTGGCGCTCTGCTCGCCGTCGGCGCTACCAAAGTGCCTAGGAATCAGGATTGGCTCGGCGTCAGCAGACAGCTCAGGACAAAGGCT
        : qp100
Segment# : 3
Offset
        : 31
1st Codon : 1
N Q D W L G V S R Q L R T K A W N R Q L Y P E W T E A O R L
AACCAAGACTGGCTGGGAGTGTCCAGGCAACTGAGAACCAAAGCCTGGAACAGACTCTACCCTGAGTGGACCGAAGCCCAAAGGCTC
        : gp100
Gene
Segment# : 4
Offset
        : 46
1st Codon : 1
 \begin{smallmatrix} W&N&R&Q&L&Y&P&E&W&T&E&A&Q&R&L&D&C&W&R&G&G&Q&V&S&L&K&V&S&N&D \end{smallmatrix} 
TGGAATAGGCAACTGTATCCCGAATGGACAGAGCTCAGAGACTGGATTGCTGGAGGGGGAGGCCAAGTGTCCCTGAAAGTGTCCAACGAT
        : gp100
Gene
Segment# : 5
Offset
        : 61
1st Codon : 1
D C W R G G Q V S L K V S N D G P T L I G A N A S F S I A L
{\tt GACTGTTGGAGAGGCGGACAGGTCAGCTCAAGGTCAGCAATGACGGACCCACACTGATTGGCGCTAACGCTTAGCATTGCCCTC}
        : gp100
Segment# : 6
        : 76
Offset
1st Codon: 1
GPTLIGANAS FSIALN FPGSQKVLPDGQVI
GGCCCTACCCTCATCGGAGCCAATGCCTCCTTCTCCATCGCTCTGAATTTCCCTGGCTCCCAGAAAGTGCTCCCCGATGGCCAAGTGATT
        : gp100
Gene
Segment# : 7
        : 91
N F P G S Q K V L P D G Q V I W V N N T I I N G S Q V W G G
AACTTTCCCGGAAGCCAAAAGGTCCTGCCTGACGGACAGGTCATCTGGGTGAATAACACAATCATTAACGGAAGCCAAGTGTGGGGCGGA
        : gp100
Gene
Segment# : 8
Offset : 106
1st Codon : 1
```

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W V N N T I I N G S Q V W G G Q P V Y P Q E T D D A C I F P $\tt TGGGTCAACAATACCATTATCAATGGCTCCCAGGTCTGGGGAGGCCCAACCCGTCTACCCTCAGGAAACCGATGACGCTTGCATTTTCCCT$ Gene : gp100 Segment# : 9 Offset : 121 1st Codon : 1 Q P V Y P Q E T D D A C I F P D G G P C P S G S W S Q K R S $\tt CAGCCTGTGTATCCCCAAGAGACAGACGATGCCTGTATCTTTCCCGATGGCGGACCCTGTCCCTCCGGCTCCTGGTCCCAGAAAAGGTCC$ Gene : gp100 Segment# : 10 Offset : 136 1st Codon: 1 D G G P C P S G S W S Q K R S F V Y V W K T W G Q Y W Q V L ${\tt GACGGAGGCCCTTGCCCTAGCGGAAGCTGGAGCCAAAAGAGAAGCTTTGTGTATGTGTGGAAGACATGGGGACAGTATTGGCAAGTGCTC}$ Gene : qp100 Segment# : 11 : 151 Offset 1st Codon : 1 F V Y V W K T W G Q Y W Q V L G G P V S G L S I G T G R A M Gene : gp100 Segment# : 12 Offset : 166 1st Codon : 1 G G P V S G L S I G T G R A M L G T H T M E V T V Y H R R G Gene : gp100 Segment# : 13 Offset : 181 L G T H T M E V T V Y H R R G S R S Y V P L A H S S S A F T Gene : gp100 Segment# : 14 Offset : 196 1st Codon : 1 S R S Y V P L A H S S S A F T I T D Q V P F S V S V S Q L R AGCAGAAGCTATGTGCCTCTGGCTCAGCTCCGGCCTTTACCATTACCGATCAGGTCCCCTTTAGCGTCAGCGTCAGCCAACTGAGAGene : gpl00 Segment# : 15 Offset : 211 1st Codon : 1 I T D Q V P F S V S V S Q L R A L D G G N K H F L R N Q P L Gene : gp100 Segment# : 16 Offset : 226 1st Codon : 1 A L D G G N K H F L R N Q P L T F A L Q L H D P S G Y L A E Gene : gp100 Segment# : 17 Offset : 241 1st Codon : 1 T F A L Q L H D P S G Y L A E A D L S Y T W D F G D S S G T : gp100 Segment# : 18 offset : 256 1st Codon : 1 A D L S Y T W D F G D S S G T L I S R A L V V T H T Y L E P

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Gene : gp100 Segment# : 19 : 271 Offset 1st Codon : 1 LISRALVVTHTYLEPGPVTAQVVLQAAIPL $\tt CTGATTAGCAGAGCCCTCGTGGTCACCCATACCTATCTGGAACCCGGACCCGTCACCGCTCAGGTCGTGCTCCAGGCTGCCATTCCCCTC$: gp100 Segment# : 20 Offset : 286 1st Codon : 1 G P V T A Q V V L Q A A I P L T S C G S S P V P G T T D G H GGCCCTGTGACAGCCCAAGTGGTCCTGCAAGCCGCTATCCCTCTGACAAGCTGTGGCTCCAGCCCTGTGCCTGGCACAACCGATGGCCAT Gene : gp100 Segment# : 21 Offset : 301 1st Codon : 1 T S C G S S P V P G T T D G H R P T A E A P N T T A G Q V P ACCTCCTGCGGAAGCTCCCCGGAACCACAGACGGACCACAGACCCACAGCCCTAACACAACCGCTGGCCAAGTGCCT Gene : gp100 Segment# : 22 : 316 Offset 1st Codon : 1 R P T A E A P N T T A G Q V P T T E V V G T T P G Q A P T A $\tt AGGCCTACCGCTGAGGCTCCCAATACCACAGCCGGACAGGTCCCCACAACCGAAGTGGTCGGCACACCCCTGGCCAAGCCCCTACCGCT$ Gene Segment# : 23 : 331 Offset 1st Codon : 1 T T E V V G T T P G Q A P T A E P S G T T S V Q V P T T E V ACCACAGAGTCGTGGGAACCACACCCGGACAGGCTCCCACAGCCGAACCCTCCGGCACAGTGCCTACCACAGAGGTC : qp100 Segment# : 24 Offset : 346 E P S G T T S V Q V P T T E V I S T A P V Q M P T A E S T G GAGCCTAGCGGAACCACAAGCGTCCCAGGTCCCCACAACCGAAGTGATTAGCACAGCCCCTGTGCAAATGCCTACCGCTGAGTCCACCGGA Gene : gp100 Segment# : 25 Offset : 361 1st Codon : 1 $\begin{smallmatrix} \begin{smallmatrix} 1 \end{smallmatrix} \begin{smallmatrix} S \end{smallmatrix} \begin{smallmatrix} T \end{smallmatrix} \begin{smallmatrix} A \end{smallmatrix} \begin{smallmatrix} P \end{smallmatrix} \begin{smallmatrix} V \end{smallmatrix} \begin{smallmatrix} Q \end{smallmatrix} \begin{smallmatrix} M \end{smallmatrix} \begin{smallmatrix} P \end{smallmatrix} \begin{smallmatrix} T \end{smallmatrix} \begin{smallmatrix} A \end{smallmatrix} \begin{smallmatrix} E \end{smallmatrix} \begin{smallmatrix} S \end{smallmatrix} \begin{smallmatrix} T \end{smallmatrix} \begin{smallmatrix} G \end{smallmatrix} M \end{smallmatrix} \begin{smallmatrix} T \end{smallmatrix} \begin{smallmatrix} P \end{smallmatrix} \begin{smallmatrix} E \end{smallmatrix} \begin{smallmatrix} K \end{smallmatrix} V \end{smallmatrix} \begin{smallmatrix} P \end{smallmatrix} V \end{smallmatrix} S \end{smallmatrix} \begin{smallmatrix} E \end{smallmatrix} V \end{smallmatrix} M \end{smallmatrix} \begin{smallmatrix} G \end{smallmatrix} \begin{smallmatrix} T \end{smallmatrix} \begin{smallmatrix} T \end{smallmatrix}$: gp100 Gene Segment# : 26 Offset : 376 M T P E K V P V S E V M G T T L A E M S T P E A T G M T P A $\tt ATGACACCCGAAAAGGTCCCCGTCAGCGAAGTGATGGGCACAACCCTCGCCGAAATGTCCACCCCTGAGGCTACCGGAATGACACCCGGT$: gp100 Gene Segment# : 27 Offset : 391 1st Codon : 1 $\begin{smallmatrix} \mathbf{L} \end{smallmatrix} \ \mathsf{A} \ \mathsf{E} \ \mathsf{M} \ \mathsf{S} \ \mathsf{T} \ \mathsf{P} \ \mathsf{E} \ \mathsf{A} \ \mathsf{T} \ \mathsf{G} \ \mathsf{M} \ \mathsf{T} \ \mathsf{P} \ \mathsf{A} \ \mathsf{E} \ \mathsf{V} \ \mathsf{S} \ \mathsf{I} \ \mathsf{V} \ \mathsf{V} \ \mathsf{L} \ \mathsf{S} \ \mathsf{G} \ \mathsf{T} \ \mathsf{T} \ \mathsf{A} \ \mathsf{A} \ \mathsf{Q} \ \mathsf{V}$ $\tt CTGGCTGAGATGAGCACACCCGAAGCCACAGGCATGACCCCTGCCGAAGTGTCCATCGTGCTCAGCGGAACCACAGCCGCTCAGGTC$ Gene : gp100 Segment# : 28 Offset : 406 1st Codon : 1

Gene : gp100

EVSIVVLSGTTAAQVTTTEWVETTAR_{ELPI}

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Segment# : 29 Offset : 421 1st Codon : 1 T T T E W V E T T A R E L P I P E P E G P D A S S I M S T E ACCACAACCGAATGGGTCGAGACAACCGCTAGGGAACTGCCTATCCCTGAGCGTGAGGGACCCGATGCCTCCAGCATTATGTCCACCGAA Gene : gp100 Segment# : 30 Offset : 436 1st Codon: 1
PEPEGPDASSIMSTESITGSLGPLLDGTAT Gene : gp100 Segment# : 31 Offset : 451 1st Codon : 1 S I T G S L G P L L D G T A T L R L V K R Q V P L D C V L Y A G CATTACCGGAAGCCTCGGCCCTCTGCTCGACGGAACCGCTACCCTCAGGCTCGTGAAAAGGCAAGTGCCTCTGGATTGCGTCCTGTAT: gp100 Segment# : 32 Offset : 466 1st Codon : 1 L R L V K R Q V P L D C V L Y R Y G S F S V T L D I V Q G I $\tt CTGAGACTGGTCAAGAGACAGGTCCCCTCGACTGTGTGTCTCTACAGATACGGAAGCTTTAGCGTCACCCTCGACATTGTGCAAGGCATT$ Gene : gp100 Segment# : 33 : 481 Offset 1st Codon : 1 R Y G S F S V T L D I V Q G I E S A E I L O A V P S G E G D : gp100 Segment# : 34 Offset : 496 1st Codon : 1 E S A E I L Q A V P S G E G D A F E L T V S C Q G G L P K E GAGTCCGCCGAAATCCTCCAGGCTGTGCCTAGCGGAGAGGGGAGACGCTTTCGAACTGACAGTGTCCTGCCAAGGCGGACTGCCTAAGGAA Gene : gp100 Segment# : 35 : 511 Offset A F E L T V S C Q G G L P K E A C M E I S S P G C O P P A O GCCTTTGAGCTCACCGTCAGCTGTCAGGGAGGCCTCCCCAAAGAGGGCTTGCATGGAGATTAGCTCCCCCGGATGCCAACCCCCTGCCCAA : gp100 Segment# : 36 : 526 Offset 1st Codon : 1 A C M E I S S P G C Q P P A Q R L C Q P V L P S P A C Q L V Gene : gp100 Segment# : 37 Offset : 541 1st Codon : 1 R L C Q P V L P S P A C Q L V L H Q I L K G G S G T Y C L N : gp100 Segment# : 38 Offset : 556 1st Codon : 1 L H Q I L K G G S G T Y C L N V S L A D T N S L A V V S T Q

Figure 27 (Cont)

: gp100

Gene

Segment# : 39 Offset : 571

155/216

1st Codon: 1 V S L A D T N S L A V V S T Q L I M P G Q E A G L G Q V P L GTGTCCCTGGCTGACACAAACTCCCTGGCTGTGGTCAGCACACAGCTCATCATGCCCGGACAGGAAGCCGGACTGGGACAGGTCCCCCTC Gene : gp100 Segment# : 40 Offset : 586 1st Codon : 1 LIMPGQEAGLGQVPLIVGILLVLMAVVLAS : gp100 Segment# : 41 Offset : 601 1st Codon : 1 I V G I L L V L M A V V L A S L I Y R R R L M K O D F S V P $\tt ATCGTCGGCATTCTGCTCGTGCTCATGGTCCTGGCTAGCCTCATCTATAGGAGAGGCTCATGAAACAGGATTTCTCCGTGCCT$: gp100 Segment# : 42 Offset : 616 1st Codon : 1 LIYRRRLMKQDFSVPQLPHSSSHWLRLPR $\tt CTGATTTACAGAAGGAGACTGATGAAGCAAGACTTTAGCGTCCCCCAACTGCCTCACTCCAGCTCCCACTGGCTGAGACTGCCTAGGATT$ Gene : qp100 Segment# : 43 Offset : 631 1st Codon : 1 Q L P H S S S H W L R L P R I F C S C P I G E N S P L L S G Gene : gp100 Segment# : 44 Offset : 646 TTCTGTAGCTGTCCCATTGGCGAAAACTCCCCCCTCCTGTCCGGCCAACAGGTCGCCGCT : MART Gene Segment# : 1 Offset : 1 1st Codon : 1 A A M P R E D A H F I Y G Y P K K G H G H S Y T T A E E A A ${\tt GCCGCTATGCCTAGGGAAGACGCTCACTTTATCTATGGCTATCCCAAAAAGGGACACTGCTACACAACCGCTGAGGAAGCCGCT}$ Gene : MART Segment# : 2 Offset : 16 1st Codon : 1 K K G H G H S Y T T A E E A A G I G I L T V I L G V L L L I AAGAAAGGCCATGGCCATAGCTATACCACAGCCGAAGAGGCTGCCGGAATCGGAATCCTCACCGTCATCCTCGGCCGTCCTGCTCCTGATT Gene : MART Segment# : 3 Offset : 31 1st Codon : 1 G I G I L T V I L G V L L L I G C W Y C R R R N G Y R A L M GGCATTGGCATTCTGACAGTGATTCTGGGAGTGCTCCTGCTCATCGGATGCTGGTACTGTAGGAGAAGGAATGGCTATAGGGCTCTGATG : MART Segment# : 4 Offset : 46 1st Codon : 1 G C W Y C R R R N G Y R A L M D K S L H V G T Q C A L T R R GGCTGTTGGTATTGCAGAAGGAGAAACGGATACAGAGCCCTCATGGATAAGTCCCTGCATGTGGGAACCCAATGCGCTCTGACAAGGAGA Gene · MART Segment# : 5 Offset : 61 1st Codon : 1 $\begin{smallmatrix} D&K&S&L&H&V&G&T&Q&C&A&L&T&R&R&C&P&Q&E&G&F&D&H&R&D&S&K&V&S&L \end{smallmatrix}$

156/216

Gene : MART
Segment# : 6
Offset : 76
1st Codon : 1
C P Q E G F

C P Q E G F D H R D S K V S L Q E K N C E P V V P N A P P A TGCCCTCAGGAAGGCTTTGACCATAGGGATAGCAAAGTGTCCCTGCAAGAGAAAAACTGTGAGCCTGTGGTCCCCAATGCCCCTCCCGCT

Gene : MART
Segment# : 7
Offset : 91
1st Codon : 1

Q E K N C E P V V P N A P P A Y E K L S A E Q S P F P Y S P CAGGAAAAGAATTGCGAACCGTCGTGCCTAACGCTCCCCTATGAGAAACTGTCCGCCGAACAGTCCCCCCTATAGCCCT

Gene : MAR' Segment# : 8 Offset : 106 1st Codon : 1

Y E K L S A E Q S P P P Y S P A A TACGAAAAGCTCAGCGCTGAGCAAAGCCCTCCCCTTACTCCCCCGCTGCC

Gene : TRP-1
Segment# : 1
Offset : 1
1st Codon : 1

A A P A F L T W H R Y H L L R L E K D M Q E M L Q E P S,F S GCCGCTCCCGCTTTCCTCACCTGGCACAGATACCATCTGCTCAGGCTCGAGAAAGACATGCAGGAAATGCTCCAGGAACCCTCCTTCTCC

Gene : TRP-1 Segment# : 2 Offset : 16 1st Codon : 1

Gene : TRP-1
Segment# : 3
Offset : 31
1st Codon : 1

L P Y W N F A T G K N V C D I C T D D L M G S R S N F D S T CTGCCTTACTGGAACTTTGCCACAGGCAAAAACGTCTGCGATATCTGTACCGATGACCTCATGGGAAGCAGAAGCAATTTCGATAGCACA

Gene : TRP-1
Segment# : 4
Offset : 46
1st Codon : 1

C T D D L M G S R S N F D S T L I S P N S V F S Q W R V V C ${\tt TGCACAGACGATCTGATGGGCTCCAGGTCCAACTTTGACTCCACCCTCATCTCCCCCAATAGCGTCTTCTCCCAGTGGAGGGTCGTGTGT$

Gene : TRP-1 Segment# : 5 Offset : 61 1st Codon : 1

L I S P N S V F S Q W R V V C D S L E D Y D T L G T L C N S CTGATTAGCCCTAACTCCGTGTTTAGCCAATGGAGAGTGGTCTGCGATAGCCTCGAGGATTACGATACCCTCGGCACACTGTGTAACTCC

Gene : TRP-1 Segment# : 6 Offset : 76 1st Codon : 1

Gene : TRP-1
Segment# : 7
Offset : 91
1st Codon : 1

T E D G P I R R N P A G N V A R P M V Q R L P E P Q D V A Q ACCGAAGACGCATTAGGAGAAACCCTGCCGGAAACGTCGCCAGACCCCATGGTGCAAAGGCTCCCCGAACCCCAAGACGTCGCCAA

157/216

Gene : TRP-1
Segment# : 8
Offset : 106
1st Codon : 1

R P M V Q R L P E P Q D V A Q C L E V G L F D T P P F Y S N AGGCCTATGGTCCAGAGACTGCCTGAGCCTCAGGATGTGCTTGGAAGTGGGACTGTTTGACACACCCCCTTTCTATAGCAAT

Gene : TRP-1 Segment# : 9 Offset : 121 1st Codon : 1

C L E V G L F D T P P F Y S N S T N S F R N T V E G Y S D P TGCCTCGAGGGTCGGCCTCTTCGATACCCTCCTTTTACTCCAACTCCACCAATAGCTTTAGGAATACCGTCGAGGGATACTCCGACCCT

Gene : TRP-1 Segment# : 10 Offset : 136 1st Codon : 1

S T N S F R N T V E G Y S D P T G K Y D P A V R S L H N L A AGCACAAACTCCTTCAGAAACACAGTGGAAGGCTATAGCGATCCCACAGGCAAATACGATCCCGCTGTGAGAAGCCTCCACAATCTGGCT

Gene : TRP-1 Segment# : 11 Offset : 151 1st Codon : 1

Gene : TRP-1 Segment# : 12 Offset : 166 1st Codon : 1

H L F L N G T G G Q T H L S S Q D P I F V L L H T F T D A V CACCTCTTCCTCAACGGAACCGAAACCCATCTGTCCAGCCAAGACCCTATCTTTGTGCTCCTGCATACCTTTACCGATGCCGTC

Gene : TRP-1 Segment# : 13 Offset : 181 1st Codon : 1

Q D P I F V L L H T F T D A V F D E W L R R Y N A D I S T F CAGGATCCCATTTCGTCCTGCTCCACCACATTCACAGACGCTGTTTTGACGAATGGCTCAGGAGATACAATGCCGATATCTCCACCTTT

Gene : TRP-1 Segment# : 14 Offset : 196 1st Codon : 1

Gene : TRP-1 Segment# : 15 Offset : 211 1st Codon : 1

PLENAPIGHNRQYNMVPFWPPVTNTEMFVTCCCCTCGGGACACCCAATGCCGACAATGTTTGTGACA

Gene : TRP-1 Segment# : 16 Offset : 226 1st Codon : 1

Gene : Tyros Segment# : 1 Offset : 1 1st Codon : 1

A A M L L A V L Y C L L W S F Q T S A G H F P R A C V S S K GCCGCTATGCTCCTGGCTGTGCTCTGGTCCTGGCAAACCTCCGGCGGACACTTTCCCAGAGCCTGTGTGTCCAGCAAA

Gene : Tyros Segment# : 2

158/216 Offset : 16 1st Codon : 1 Q T S A G H F P R A C V S S K N L M E K E C C P P W S G D R CAGACAAGCGCTGGCCATTTCCCTAGGGCTTGCGTCAGCTCCAAGAATCTGATGAGAAAAGAGTGTTGCCCTCCTGGAGGGGAGACAGA Gene : Tyros Segment# : 3 Offset : 31 1st Codon : 1 N L M E K E C C P P W S G D R S P C G Q L S G R G S C Q N I AACCTCATGGAAAAGGAATGCTGTCCCCCTTGGTCCGGCAAACGTCCCCCTGTGGCCAAACTGTCCGGCAGAGGCTCCTGCCAAAACATT Gene : Tyros Segment# : 4 Offset : 46 1st Codon : 1 S P C G Q L S G R G S C Q N I L L S N A P L G P Q F P F T G $\tt AGCCCTTGCGGACAGCTCAGCGGAAGGGGAAGCTGTCAGAATATCCTCCTGTCCAACGCTCCCCTCGGCCCTCAGTTTCCCTTTACCGGA$ Gene : Tyros Segment# : 5 Offset : 61 1st Codon : 1 L L S N A P L G P Q F P F T G V D D R E S W P S V F Y N R T Gene : Tyros Segment# : 6 Offset : 76 V D D R E S W P S V F Y N R T C Q C S G N F M G F N C G N C $\tt GTGGATGACAGAGAGTCCTGGCCTAGCGTCTTCTATAACAGAACCTGTCAGTGTAGCGGAAACTTTATGGGATTCAATTGCGGAAACTGT$ Gene : Tyros Segment# : 7 Offset : 91 1st Codon : 1 C Q C S G N F M G F N C G N C K F G F W G P N C T E R R L L $\tt TGCCAATGCTCCGGCAATTTCATGGGCTTTAACTGTGGCAATTGCAAATTCGGATTCTGGGGCCCTAACTGTACCGAAAGGAGACTGCTC$: Tyros Gene Segment# : 8 Offset : 106 K F G F W G P N C T E R R L L V R R N I F D L S A P E K D K ${\tt AAGTTTGGCTTTTGGGGACCCAATTGCACAGAGAGAGAGGCTCCTGGTCAGGAGAAACATTTTCGATCTGTCCGCCCCTGAGAAAGACAAA$ Gene : Tyros Segment# : 9 Offset : 121 1st Codon: 1 V R R N I F D L S A P E K D K F F A Y L T L A K H T I S S D GTGAGAAGGAATATCTTTGACCTCAGCGCTCCCGAAAAGGATAAGTTTTTCGCTTACCTCACCCTCGCCAAACACACAATCTCCAGCGAT Gene : Tvros Segment# : 10 Offset : 136 1st Codon : 1 FFAYLTLAKHTISSDYVIPIGTYGQMKNGS ${\tt TTCTTTGCCTATCTGACACTGGCTAAGCATACCATTAGCTCCGACTATGTGATTCCCATTGGCACATACGGACAGATGAAGAATGGCTCC}$ Gene : Tyros Segment# : 11 Offset : 151 1st Codon : 1 Y V I P I G T Y G Q M K N G S T P M F N D I N I Y D L F V W

Gene : Tyros Segment# : 12 Offset : 166 1st Codon : 1

159/216

T P M F N D I N I Y D L F V W M H Y Y V S M D A L L G G S E ACCCCTATGTTTAACGATATCAATATCTATGACCTCTTCGTCTGGATGCACTATTACGTCAGCATGGACGCTCTGCTCGGCGGAAGCGAA Gene : Tyros Segment# : 13 : 181 Offset 1st Codon : 1 MHYYVSMDALLGGSEIWRDIDFAHEAPAFL ATGCATTACTATGTGTCCATGGATGCCCTCCTGGGAGGCTCCGAGATTTGGAGAGACATTGACTTTGCCCATGAGGCTCCCGCTTTCCTC : Tyros Gene Segment# : 14 Offset : 196 1st Codon : 1 I W R D I D F A H E A P A F L P W H R L F L L R W E Q E I Q $\tt ATCTGGAGGGATATCGATTTCGCTCACGAAGCCCCTGCCTTTCTGCCTTGGCATAGGCTCTTCCTCCTGAGATCGGAACAGGAAATCCAA$ Gene : Tyros Segment# : 15 Offset : 211 1st Codon : 1 PWHRLFLLRWEQEIQKLTGDENFTIPYWDW $\tt CCCTGGCACAGACTGTTTCTGCTCAGGTGGGAGCAAGAGATTCAGAAACTGACAGGCGATGAGAATTTCACAATCCCTTACTGGGACTGG$ Gene : Tyros Segment# : 16 Offset : 226 K L T G D E N F T I P Y W D W R D A E K C D I C T D E Y M G Segment# : 17 Offset : 241 1st Codon : 1 R D A E K C D I C T D E Y M G G Q H P T N P N L L S P A S F AGGGATGCCGAAAAGTGTGACATTTGCACAGACGAATACATGGGCGGACAGCATCCCACAAACCCTAACCTCCTGTCCCCCGCTAGCTTT Gene : Tyros Segment# : 18 Offset : 256 G Q H P T N P N L L S P A S F F S S W Q I V C S R L E E Y N GGCCAACACCCTACCAATCCCAATCTGCTCAGCCCTGCCTCCTTCTTTAGCTCCTGGCAAATCGTCTGCTCCAGGCTCGAGGAATACAAT : Tyros Segment# : 19 : 271 Offset 1st Codon : 1 FSSWQIVCSRLEEYNSHQSLCNGTPEGPLR : Tyros Gene Segment# : 20 Offset : 286 1st Codon : 1 SH Q S L C N G T P E G P L R R N P G N H D K S R T P R L P AGCCATCAGTCCCTGTGTAACGGAACCCCTGAGGGACCCCTCAGGAGAAACCCTGGCAATCACGATAAGTCCAGGACACCCAGACTGCCT: Tyros Segment# : 21 Offset : 301 1st Codon : 1 RNPGNHDKSRTPRLPSSADVEFCLSLTQYE AGGAATCCCGGAAACCATGACAAAAGCAGAACCCCTAGGCTCCCCTCCAGCGCTGACGTCGAGTTTTGCCTCAGCCTCACCCAATACGAA : Tyros Gene Segment# : 22 Offset : 316 1st Codon : 1 S S A D V E F C L S L T Q Y E S G S M D K A A N F S F R N T AGCTCCGCCGATGTGGAATTCTGTCTGTCCCTGACACAGTATGAGTCCGGCTCCATGGATAAGGCTGCCAATTTCTCCTTCAGAAACACA

160/216

: Tyros Segment# : 23 Offset : 331 1st Codon : 1 S G S M D K A A N F S F R N T L E G F A S P L T G I A D A S AGCGGAAGCATGGACAAAGCCGCTAACTTTAGCTTTAGGAATACCCTCGAGGGATTCGCTAGCCCTCTGACAGGGATTGCCGATGCCTCC Gene : Tyros Segment# : 24 : 346 Offset 1st Codon : 1 LEGFASPLTGIADASQSSMHNALHIYMNGT : Tyros Gene Segment# : 25 Offset : 361 1st Codon : 1 Q S S M H N A L H I Y M N G T M S Q V Q G S A N D P I F L L Gene : Tyros Segment# : 26 Offset : 376 1st Codon : 1 M S Q V Q G S A N D P I F L L H H A F V D S I F E Q W L Q R ATGTCCCAGGTCCAGGGAAGCGCTAACGATCCCATTTTCCTCCTGCATCACGCTTTCGTCGACTCCATCTTTGAGCAATGGCTCCAGAGA Gene : Tyros Segment# : 27 Offset. : 391 H H A F V D S I F E Q W L Q R H R P L Q E V Y P E A N A P I $\tt CACCATGCCTTTGTGGATAGCATTTCGAACAGTGGCTGCAAAGGCATAGGCCTCTGCAAGAGGTCTACCCTGAGGCTAACGCTCCCATT$: Tyros : 28 Segment# Offset : 406 1st Codon : 1 Gene : Tyros Segment# : 29 Offset : 421 1st Codon : 1 G H N R E S Y M V P F I P L Y R N G D F F I S S K D L G Y D $\tt GGCCATAACAGAGAGTCCTACATGGTGCCTTTCATTCCCCTCTACAGAAACGGAGACTTTTTCATTAGCTCCAAGGATCTGGGATACGAT$: Tyros Segment# : 30 Offset : 436 1st Codon : 1 RNGDFFISSKDLGYDYSYLQDSDPDSF_QDY AGGAATGGCGATTTCTTTATCTCCAGCAAAGACCTCGGCTATGACTATAGCTATCTGCAAGACTCCGACCCTGACTCCTACGAGACTAT Gene : Tyros Segment# : 31 Offset : 451 1st Codon : 1 Y S Y L Q D S D P D S F Q D Y I K S Y L E Q A S R I W S W ${\tt TACTCCTACCTCCAGGATAGCGATCCCGATAGCTTTCAGGATTACATTAAGTCCTACCTCGAGCAAGCCTCCAGGATTTGGTCCTGGCTCCAGGATTTAAGTTCCTACCTCGAGCAAGCCTCCAGGATTTGGTCCTGGCTCCAGGATTTGGTCCTGGCTCCAGGATTTGGTCCTGGCTCCAGGATTTGGTCCTGGCTCCAGGATTTAAGTTCCTACCTCGAGCAAGCCTCCAGGATTTGGTCCTGGCTCCAGGATTTAAGTTCCTACCTCGAGCAAGCCTCCAGGATTTGGTCCTGGCTCCAGGATTTAAGTTCCTACCTCGAGCAAGCCTCCAGGATTTGGTCCTGGCTCCAGGATTTAAGTTCCTACCTCAGGATTTGGTCCTGGCTCCAGGATTAAGCTCCTGAGATTAAGTTCCTAGCTCAGGATTTGGTCCTGGCTCCAGGATTTGGTCCTGGCTCCAGGATTAAGTTCAGGTCCTGAGATTAAGTTCTAGTCTAGGTCTAGGTCTAGGTTTAAGTTCTAGGTCTAGGTTTAAGTTCTAGGTCTAGGTTTAGATTAAGTTCTAGGTCCTGGCTCAGGATTTGGTCCTGGCTCAGGATTAGATTAAGTTCTAGTTAGATTAAGTTCTAGATTAAGATTAAGTTCTAGATTAAGATT$ Gene : Tyros Segment# : 32 Offset : 466 1st Codon : 1 I K S Y L E Q A S R I W S W L L G A A M V G A V L T A L L A

Figure 27 (Cont)

Gene

: Tyros

161/216 Segment# : 33 Offset : 481 1st Codon : 1 L G A A M V G A V L T A L L A G L V S L L C R H K R K O L P $\tt CTGGGAGCCGCTATGGTCGGCGCTGTGCTCACCGCTCTGCTCGCCGGACTGGTCAGCCTCCTGTGTAGGCATAAGAGAAAGCAACTGCCT$ Gene : Tyros Segment# : 34 Offset : 496 1st Codon: 1
G L V S L L C R H K R K Q L P E E K Q P L L M E K E D Y H S ${\tt GGCCTCGTGTCCCTGCAGACACAAAAGGAAACAGCTCCCCGAAGAGAAACAGCCTCTGCTCATGGAAAAGGAAGACTATCACTCC}$: Tyros Segment# : 35 Offset : 511 1st Codon : 1 EEKQPLLMEKEDYHSLYQSHLAA GAGGAAAAGCAACCCCTCCTGATGGAGAAAGAGGATTACCATAGCCTCTACCAAAGCCATCTGGCTGCC : TRP2 Segment# : 1 Offset : 1 1st Codon: 1 A A M S P L W W G F L L S C L G C K I L P G A Q G Q F P R V ${\tt GCCGCTATGTCCCCCCTCTGGTGGGGCTTTCTGCTCAGCTGTCTGGGATGCAAAATCCTCCCGGAGCCCAAGGCCAAGTTCCCTAGGGTCCCAAGGCCCCAAGGCCCAAGGCCCAAGGCCCCAAGGCCCCAAGGCCCCAAGGCCCCAAGGCCCCAAGGCCCAAGGCCCAAGGCCCAAGGCCCAAGGCCCAAGGCCCAAGGCCCAAGGCCCCAAGGCCCCAAGGCCCCAAGGCCCCAAGGCCCCAAGGCCCCAAGGCCCCAAGGCCCCAAGGCCCCAAGGCCCCAAGGCCCCAAGGCCCCAAGGCCCCA$: TRP2 Gene Segment# : 2 : 16 1st Codon: 1 GCKILPGAQGQFPRVCMTVDSLVNKECCPR GGCTGTAAGATTCTGCCTGGCGCTCAGGGACAGTTTCCCAGAGTGTGTATGACAGTGGATAGCCTCGTGAATAAGGAATGCTGTCCCAGA : TRP2 Segment# : 3 Offset : 31 1st Codon : 1 $\begin{smallmatrix} C&M&T&V&D&S&L&V&N&K&E&C&C&P&R&L&G&A&E&S&A&N&V&C&G&S&Q&Q&G&R\\ \end{smallmatrix}$ Gene : TRP2 Segment# : 4 LGAESANVCGSQQGRGQCTEVRADTRPWSG Gene : TRP2 Segment# : 5 Offset. : 61 1st Codon : 1 G Q C T E V R A D T R P W S G P Y I L R N O D D R E L W P R GGCCAATGCACAGAGGTCAGGGCTGACACAAGGCCTTGGTCCGGCCCTTACATTCTGAGAAACCAAGACGATAGGGAACTGTGGCCCAGA : TRP2 Gene Segment# : 6 : 76 Offset 1st Codon : 1 PYILRNQDDRELWPRKFFHRTCKCTGNFAG CCCTATATCCTCAGGAATCAGGATGACAGAGAGCTCTGGCCTAGGAAATTCTTTCACAGAACCTGTAAGTGTACCGGAAACTTTGCCGGA Gene : TRP2 Segment# : 7 : 91 Offset K F F H R T C K C T G N F A G Y N C G D C K F G W T G P N C ${\tt AAGTTTTCCATAGGACATGCAAATGCACAGGCAATTTCGCTGGCTATAACTGTGGCGATTGCAAATTCGGATGGACAGGCCCTAACTGT}$

: TRP2 Gene Segment# : 8 : 106 Offset

162/216 1st Codon : 1 Y N C G D C K F G W T G P N C E R K K P P V I R Q N I H S L Gene : TRP2 Segment# : 9 Offset : 121 1st Codon : 1 E R K K P P V I R Q N I H S L S P Q E R E Q F L G A L D L A : TRP2 Segment# : 10 Offset : 136 1st Codon : 1 S P Q E R E Q F L G A L D L A K K R V H P D Y V I T T O H W : TRP2 Gene Segment# : 11 Offset : 151 1st Codon : 1 K K R V H P D Y V I T T Q H W L G L L G P N G T Q P Q F A N AAGAAAAGGGTCCACCCTGACTATGTGATTACCACACAGCATTGGCTCGGCCTCCTGGGACCCAATGGCACACAGCCTCAGTTTGCCAAT : TRP2 Gene Segment# : 12 Offset : 166 1st Codon : 1 L G L L G P N G T Q P Q F A N C S V Y D F F V W L H Y Y S V $\tt CTGGGACTGCTCGGCCCTAACGGAACCCCAACTCGCTAACTGTAGCGTCTACGATTTCTTTGTGTGGCTGCATTACTATAGCGTC$ Gene : TRP2 Segment# : 13 Offset : 181 1st Codon : 1 $\begin{smallmatrix} C & S & V & Y & D & F & F & V & W & L & H & Y & Y & S & V & R & D & T & L & G & P & G & R & P & Y & R & A & I & D \\ \end{smallmatrix}$ TGCTCCGTGTATGACTTTTTCGTCTGGCTCCACTATTACTCCGTGAGAGACACTGCTCGGCCCTGGCAGACCCTATAGGGCTATCGAT Gene : TRP2 Segment# : 14 Offset : 196 1st Codon : 1 R D T L L G P G R P Y R A I D F S H O G P A F V T W H R Y H ${\tt AGGGATACCCTCCTGGGACCCGGAAGGCCTTACAGAGCCATTGACTTTAGCCATCAGGGACCCGCTTTCGTCACCTGGCACAGATACCAT}$: TRP2 Gene Segment# : 15 Offset : 211 1st Codon : 1 F S H Q G P A F V T W H R Y H L L C L E R D L Q R L I G N E ${\tt TTCTCCCACCAAGGCCCTGCTTTGTGACATGGCATAGGTATCACCTCCTGTGTCTGGAAAGGGATCTGCAAAGGCTCATCGGAAACGAA}$: TRP2 Gene Segment# : 16 Offset : 226 1st Codon : 1 L L C L E R D L Q R L I G N E S F A L P Y W N F A T G R N E $\tt CTGCTCTGCCTCGAGAGAGACCTCCAGAGACTGATTGGCAATGAGTCCTTCGCTCTGCCTTACTGGAACTTTGCCACAGGCAGAAACGAA$: TRP2 Segment# : 17 Offset : 241 1st Codon : 1 S F A L P Y W N F A T G R N E C D V C T D Q L F G A A R P D : TRP2 Gene Segment# : 18 Offset : 256 1st Codon : 1

Figure 27 (Cont)

 $\texttt{C} \ \ \texttt{D} \ \ \texttt{V} \ \ \texttt{C} \ \ \texttt{T} \ \ \texttt{D} \ \ \texttt{Q} \ \ \texttt{L} \ \ \texttt{F} \ \ \texttt{G} \ \ \texttt{A} \ \ \texttt{A} \ \ \texttt{P} \ \ \texttt{D} \ \ \texttt{D} \ \ \texttt{P} \ \ \texttt{T} \ \ \texttt{L} \ \ \texttt{I} \ \ \texttt{S} \ \ \texttt{R} \ \ \texttt{N} \ \ \texttt{S} \ \ \texttt{R} \ \ \texttt{F} \ \ \texttt{S} \ \ \texttt{W} \ \ \texttt{E}$

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DPTLISRNSRFSSWETVCDSLDDYNHLVTL GACCCTACCCTCATCTCCAGGAATAGCAGATTCTCCAGCTGGGAGACAGTGTGTGACTCCCTGGATGACTATAACCATCTGGTCACCCTC Gene : TRP2 Segment# : 20 Offset : 286

Segment# : 19 Offset

1st Codon : 1

1st Codon : 1

Gene

: TRP2

: 271

T V C D S L D D Y N H L V T L C N G T Y E G L L R R N Q M G

: TRP2 Segment# : 21 : 301 Offset 1st Codon : 1

 $\begin{smallmatrix} \mathbf{C} & \mathbf{N} & \mathbf{G} & \mathbf{T} & \mathbf{Y} & \mathbf{E} & \mathbf{G} & \mathbf{L} & \mathbf{L} & \mathbf{R} & \mathbf{R} & \mathbf{N} & \mathbf{Q} & \mathbf{M} & \mathbf{G} & \mathbf{R} & \mathbf{N} & \mathbf{S} & \mathbf{M} & \mathbf{K} & \mathbf{L} & \mathbf{P} & \mathbf{T} & \mathbf{L} & \mathbf{K} & \mathbf{D} & \mathbf{I} & \mathbf{R} & \mathbf{D} & \mathbf{C} \\ \end{smallmatrix}$ TGCAATGGCACATACGAAGGCCTCCTGAGAAGGAATCAGATGGGCAGAAACTCCATGAAACTGCCTACCCTCAAGGATATCAGAGACTGT

: TRP2 Gene Segment# : 22 Offset : 316 1st Codon : 1

R N S M K L P T L K D I R D C L S L Q K F D N P P F F Q N S

: TRP2 Gene Segment# : 23 Offset : 331 1st Codon : 1

LSLQKFDNPPFFQNSTFSFRNALEGFDKAD $\tt CTGTCCCTGCAAAAGTTTGACAATCCCCCTTTCTTTCAGAATAGCACATTCTCCTTCAGAAACGCTCTGGAAGGCTTTGACAAAGCCGAT$

Gene : TRP2 Segment# : 24 : 346 Offset

1st Codon: 1 TFSFRNALEGFDKADGTLDSQVMSLHNLVH ACCTTTAGCTTTAGGAATGCCCTCGAGGGATTCGATAAGGCTGACGGAACCCTCGACTCCCAGGTCATGTCCCTGCATAACCTCGTGCAT

Gene : TRP2 Segment# : 25 Offset : 361 1st Codon : 1

 $\texttt{G} \ \texttt{T} \ \texttt{L} \ \texttt{D} \ \texttt{S} \ \texttt{Q} \ \texttt{V} \ \texttt{M} \ \texttt{S} \ \texttt{L} \ \texttt{H} \ \texttt{N} \ \texttt{L} \ \texttt{V} \ \texttt{H} \ \texttt{S} \ \texttt{F} \ \texttt{L} \ \texttt{N} \ \texttt{G} \ \texttt{T} \ \texttt{N} \ \texttt{A} \ \texttt{L} \ \texttt{P} \ \texttt{H} \ \texttt{S} \ \texttt{A} \ \texttt{A} \ \texttt{N}$

: TRP2 Gene Segment# : 26 Offset : 376 1st Codon: 1

S F L N G T N A L P H S A A N D P I F V V L H S F T D A I F AGCTTTCTGAATGGCACAAACGCTCTGCCTCACTCCGCCGCTAACGATCCCATTTTCGTCGTGCTCCACTCCTTCACAGACGCTATCTTT

: TRP2 Gene Segment# : 27 Offset : 391 1st Codon : 1

D P I F V V L H S F T D A I F D E W M K R F N P P A D A W P GACCCTATCTTTGTGGTCCTGCATAGCTTTACCGATGCCATTTTCGATGAGTGGATGAAAAGGTTTAACCCTCCCGCTGACGCTTGGCCT

: TRP2 Segment# : 28 Offset : 406 1st Codon : 1

D E W M K R F N P P A D A W P Q E L A P I G H N R M Y N M V GACGAATGGATGAAGAGATTCAATCCCCCTGCCGATGCCTGGCCCCAAGAGCTCGCCCCTATCGGACACAATAGGATGTACAATATGGTC

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: TRP2 Gene Segment# : 29 Offset : 421 1st Codon : 1 Q E L A P I G H N R M Y N M V P F F P P V T N E E L F L T S : TRP2 Gene Segment# : 30 Offset : 436 1st Codon : 1 P F F P P V T N E E L F L T S D Q L G Y S Y A I D L P V S V $\tt CCCTTTTTCCCTCCCGTCACCAATGAGGAACTGTTTCTGACAAGCGATCAGCTTCGGCTATAGCTATGCCATTGACCTCCCCGTCAGCTCAG$: TRP2 Segment# : 31 Offset : 451 1st Codon : 1 D Q L G Y S Y A I D L P V S V E E T P G W P T T L L V V M G GACCAACTGGGATACTCCTACGCTATCGATCTGCCTGTGTCCGTGGAAGAGACACCCGGATGGCCTACCACACTGCTCGTGGTCATGGGA Gene : TRP2 Segment# : 32 : 466 E E T P G W P T T L L V V M G T L V A L V G L F V L L A F L ${\tt GAGGAAACCCCTGGCTGGCCCACAACCCTCCTGGTCGTGATGGGCACACTGGTCGCCCTCGTGGGACTGTTTTGTGCTCCTGGCTTTTCCTC}$ Gene : TRP2 Segment# : 33 Offset : 481 1st Codon : 1 T L V A L V G L F V L L A F L Q Y R R L R K G Y T P L M E T ACCCTCGTGGCTCTGGTCGGCCTCTTCGTCCTGCTCGCCATACAGAAGGCTCAGGAAAGGCTATACCCCTCTGATGGAGACA Gene : TRP2 Segment# : 34 Offset 1st Codon : 1 O Y R R L R K G Y T P L M E T H L S S K R Y T E E A A A ${\tt CAGTATAGGAGACTGAGAAAAGGGATACACACCCCTCATGGAAAACCCATCTGTCCAGCAAAAAGGTATACCGAAGAGGCTGCCGCT}$: MC1R Segment# : 1 Offset : 1 1st Codon : 1 GCCGCTATGGCTGTGCAAGGCTCCCAGAGAAGGCTCCTGGGAAGCCTCAACTCCACCCTACCGCTATCCCTCAGCTCGGCCTCGCCGCT Gene : MC1R Segment# : 2 Offset : 16 1st Codon : 1 L N S T P T A I P Q L G L A A N Q T G A R C L E V S I S D G CTGAATAGCACCCCACAGCCATTCCCCAACTGGGACTGGCTGCCAATCAGACAGGCGCTAGGTGTCTGGAAGTGTCCATCTCCGACGGA Gene : MC1R Segment# : 3 Offset : 31 N Q T G A R C L E V S I S D G L F L S L G L V S L V E N A L AACCAAACCGGAGCCAGATGCCTCGAGGTCAGCATTAGCGATGGCCTCTTCCTCAGCCTCGGCCTCGTGTCCCTGGTCGAGAATGCCCTC : MC1R Gene : 4 Segment# Offset : 46 1st Codon : 1 L F L S L G L V S L V E N A L V V A T I A K N R N L H S P M

: MC1R Gene Segment# : 5

165/216 Offset : 61 1st Codon : 1 V V A T I A K N R N L H S P M Y C F I C C L A L S D L L V S $\tt GTGGTCGCCACAATCGCTAAGAATAGGAATCTGCATAGCCCTATGTATTGCTTTATCTGTTGCCTCGCCCTCAGCGATCTGCTCGTGTCC$: MC1R Segment# : 6 Offset : 76 1st Codon: 1 Y C F I C C L.A L S D L L V S G T N V L E T A V I L L E A TACTGTTTCATTTGCTGTCTGGCTCTGTCCGACCTCCTGGTCAGCGGAACCAATGTGCTCGAGACAGCCGTCATCCTCCTGCTCGAGGCT : MC1R Gene Segment# : 7 Offset : 91 1st Codon : 1 G T N V L E T A V I L L E A G A L V A R A A V L Q Q L D N $\tt GGCACAAACGTCCTGGAAACCGCTGTGATTCTGCTCCTGGAAGCCGGAGCCCTCGTGGCTAGGGCTGCCGTCCTGCAACAGCTCGACAAT$ Segment# : 8 Offset : 106 1st Codon : 1 G A L V A R A A V L Q Q L D N V I D V I T C S S M L S S L C Gene : MC1R Segment# : 9 : 121 V I D V I T C S S M L S S L C F L G A I A V D R Y I S I F Y ${\tt GTGATTGACGTCATCACATGCTCCAGCATGCTGTCCAGCCTCTGCTTTCTGGGAGCCATTGCCGTCGACAGATACATTAGCATTTTCTATT$: MC1R Gene Segment# : 10 Offset : 136 1st Codon : 1 F L G A I A V D R Y I S I F Y A L R Y H S I V T L P R A P R : MCJR Gene Segment# : 11 1st Codon : 1 ALRYHSIVTLPRAPRAVAAIWVASVVFSTL : MCIR Segment# : 12 Offset : 166 1st Codon : 1 A V A A I W V A S V V F S T L F I A Y Y D H V A V L L C L V Gene : MC1R Segment# : 13 Offset : 181 1st Codon : 1 F I A Y Y D H V A V L L C L V V F F L A M L V L M A V L Y V Gene : MC1R Segment# : 14 Offset : 196 1st Codon : 1 V F F L A M L V L M A V L Y V H M L A R A C Q H A Q G I A R

Segment# : 15 Offset : 211 1st Codon : 1

166/216

H M L A R A C Q H A Q G I A R L H K R Q R P V H Q G F G L K ${\tt CACATGCTGGCTAGGGCTTGCCAACACGCTCAGGGAATCGCTAGGCTCCACAAAAGGCCAAAAGGCCTGTGCATCAGGGATTCGGACTGAAA}$: MC1R Segment# : 16 Offset : 226 1st Codon : 1 L H K R Q R P V H Q G F G L K G A V T L T I L L G I F F L C $\tt CTGCATAAGAGACAGGAGACCCGTCCACCAAGGCTTTGGCCTCAAGGGAGCCGTCACCCTCACCATTCTGCTCGGCATTTTCTTTTCTGTGT$: MC1R Segment# : 17 Offset : 241 1st Codon : 1 G A V T L T I L L G I F F L C W G P F F L H L T L I V L C P Gene : MC1R Segment# : 18 Offset : 256 1st Codon : 1 W G P F F L H L T L I V L C P E H P T C G C I F K N F N L F $\tt TGGGGACCCTTTTTCCTCCACCTCATCGTCCTGTGTCCCGAACACCCTACCTGTGGCTGTATCTTTAAGAATTTCAATCTGTTT$ Segment# : 19 Offset : 271 1st Codon : 1 E H P T C G C I F K N F N L F L A L I I C N A I I D P L I Y GAGCATCCCACATGCGGATGCATTTTCAAAAACTTTAACCTCTTCCTCGCCCTCATCATTTTGCAATGCCATTATCGATCCCCTCATCTAT : MC1R Gene Segment# : 20 Offset : 286 LALIICNAIIDPLIYAFHSOELRRTLKEVL $\tt CTGGCTCTGATTATCTGTAACGCTATCATTGACCCTCTGATTTACGCTTTCCATAGCCAAGAGCTCAGGAGAACCCTCAAGGAAGTGCTC$: MClR Segment# : 21 Offset : 301 1st Codon : 1 A F H S Q E L R R T L K E V L T C S W A A ${\tt GCCTTTCACTCCCAGGAACTGAGAAGGACACTGAAAGAGGTCCTGACATGCTCCTGGGCTGCC}$: MUClF Gene Segment# : 1 Offset : 1 1st Codon : 1 A A M T P G T Q S P F F L L L L T V L T V V T G S G H A S : MUC1F Segment# : 2 Offset : 16 1st Codon : 1 $\texttt{L} \quad \texttt{L} \quad \texttt{T} \quad \texttt{V} \quad \texttt{L} \quad \texttt{T}^{'} \quad \texttt{V} \quad \texttt{V} \quad \texttt{T} \quad \texttt{G} \quad \texttt{S} \quad \texttt{G} \quad \texttt{H} \quad \texttt{A} \quad \texttt{S} \quad \texttt{S} \quad \texttt{T} \quad \texttt{P} \quad \texttt{G} \quad \texttt{G} \quad \texttt{E} \quad \texttt{K} \quad \texttt{E} \quad \texttt{T} \quad \texttt{S} \quad \texttt{A} \quad \texttt{T} \quad \texttt{Q} \quad \texttt{R} \quad \texttt{S}$ CTGCTCACCGTCCTGACAGTGGTCACCGGAAGCGGACACGCTAGCTCCACCCCTGGCGGAGAGAAGAGACAAGCGCTACCCAAAGGTCC Gene : MUC1F Segment# : 3 : 31 Offset 1st Codon : 1 S T P G G E K E T S A T Q R S S V P S S T E K N A V S M T S : MUCLF Gene Segment# : 4 Offset : 46 $\mathtt{S} \ \ \mathtt{V} \ \ \mathtt{P} \ \ \mathtt{S} \ \ \mathtt{T} \ \ \mathtt{E} \ \ \mathtt{K} \ \ \mathtt{N} \ \ \mathtt{A} \ \ \mathtt{V} \ \ \mathtt{S} \ \ \mathtt{M} \ \ \mathtt{T} \ \ \mathtt{S} \ \ \mathtt{V} \ \ \mathtt{L} \ \ \mathtt{S} \ \ \mathtt{S} \ \ \mathtt{H} \ \ \mathtt{S} \ \ \mathtt{P} \ \ \mathtt{G} \ \ \mathtt{S} \ \ \mathtt{S} \ \ \mathtt{T} \ \ \mathtt{T}$

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: MUC1F Segment# : 5 Offset : 61 1st Codon : 1 S V L S S H S P G S G S S T T Q G Q D V T L A P A T E P A S AGCGTCCTGTCCAGCCATAGCCCTGGCTCCGGCTCCAGCACAACCCCAAGGCCCAAGACGTCACCCTCGCCCCTGCCACAGAGCCTTGCCTCC Gene : MUC1F Segment# : 6 Offset : 76 1st Codon : 1 Q G Q D V T L A P A T E P A S G S A A T W G Q D V T S V P V $\tt CAGGGACAGGATGTGACACTGGCTCCCGCTACCGAACCCGCTAGCGGAAGCGCTGCCACATGGGGACAGGATGTGACAAGCGTCCCCGTC$: MUC1F Gene Segment# : 7 Offset : 91 1st Codon : 1 G S A A T W G Q D V T S V P V T R P A L G S T T P P A H D V : MUC1F Segment# : 8 Offset : 106 1st Codon : 1 T R P A L G S T T P P A H D V T S A P D N K A A : MUClR Gene Segment# : 1 Offset 1st Codon : 1 A A N R P A L G S T A P P V H N V T S A S G S A S G S A S T : MUCIR Segment# : 2 Offset : 16 1st Codon : 1 N V T S A S G S A S G S A S T L V H N G T S A R A T T T P A AACGTCACCTCCGCCTCCGGCTCCGGCTCCGCCTCCACCCTCGTGCATAACGGAACCTCCGCCAGAGCCACACCACCCCGCT Gene : MUC1R Segment# : 3 Offset : 31 1st Codon : 1 LVHNGTSARATTTPASKSTPFSIPSHHSDT : MUC1R Segment# : 4 Offset : 46 1st Codon : 1 S K S T P F S I P S H H S D T P T T L A S H S T K T D A S S Gene : MUC1R Segment# : 5 Offset : 61 1st Codon : 1 PTTLASHSTKTDASSTHHSSVPPLTSSNHS : MUC1R Gene Segment# : 6 : 76 Offset 1st Codon : 1 THHSSVPPLTSSNHSTSPQLSTGVSFFFLS Gene : MUC1R

168/216 Segment# : 7 Offset : 91 1st Codon : 1 T S P Q L S T G V S F F F L S F H I S N L Q F N S S L E D P ACCTCCCCCCAACTGTCCACCGGAGTGTCCTTCTTTTTCCTCAGCTTTCACATTAGCAATCTGCAATTCAATAGCTCCCTGGAAGACCCT Segment# : 8 Offset : 106 1st Codon : 1 F H I S N L Q F N S S L E D P S T D Y Y Q E L O R D I S E M TTCCATATCTCCAACCTCCAGCTTTAACTCCAGCCTCGAGGATCCCTCCACCGATTACTATCAGGAACTGCAAAGGGATATCTCCGAGATG : MUC1R Segment# : 9 Offset : 121 1st Codon : 1 S T D Y Y Q E L Q R D I S E M F L Q I Y K Q G G F L G L S N Gene : MUCLR Segment# : 10 Offset : 136 F L Q I Y K Q G G F L G L S N I K F R P G S V V V O L T L A TTCCTCCAGATTTACAAACAGGGAGGCTTTCTGGGACTGTCCAACATTAAGTTTAGGCCTGGCTCCGTGGTCGTGCAACTGACACTGGCT : MUC1R Segment# : 11 Offset : 151 1st Codon : 1 I K F R P G S V V V Q L T L A F R E G T I N V H D V E T Q F : MUC1R Gene Segment# : 12 Offset : 166 1st Codon : 1 F R E G T I N V H D V E T Q F N O Y K T E A A S R Y N L T I ${\tt TTCAGAGAGGGAACCATTAACGTCCACGATGTGGAAACCCAATTCAATCAGTATAAGACAGAGGCTGCCTCCAGGTATAACCTCACCATT}$ Segment# : 13 Offset : 181 1st Codon : 1 N Q Y K T E A A S R Y N L T I S D V S V S D V P F P F S A Q AACCAATACAAAACCGAAGCCGCTAGCAGATACAATCTGACAATCTCCGACGTCAGCGTCAGCGATGTGCCTTTCCCCTTTCTCCGCCCAA : MUC1R Gene Segment# : 14 Offset : 196 1st Codon : 1 $\texttt{S} \ \ \texttt{D} \ \ \texttt{V} \ \ \texttt{S} \ \ \texttt{D} \ \ \texttt{V} \ \ \texttt{P} \ \ \texttt{P} \ \ \texttt{F} \ \ \texttt{P} \ \ \texttt{F} \ \ \texttt{S} \ \ \texttt{A} \ \ \texttt{Q} \ \ \texttt{S} \ \ \texttt{G} \ \ \texttt{A} \ \ \texttt{G} \ \ \texttt{V} \ \ \texttt{P} \ \ \texttt{G} \ \ \texttt{W} \ \ \texttt{G} \ \ \texttt{I} \ \ \texttt{A} \ \ \texttt{L} \ \ \texttt{L} \ \ \texttt{V} \ \ \texttt{L}$ AGCGATGTGTCCGTGTCCCGACGTCCCCTTTCCCTTTAGCGCTCAGTCCGGCGCTGGCGTCCCCGGATGGGGAATCGCTCTGCTCGTGCTC : MUC1R Segment# : 15 Offset : 211 1st Codon : 1 $\mathtt{S} \ \mathtt{G} \ \mathtt{A} \ \mathtt{G} \ \mathtt{V} \ \mathtt{P} \ \mathtt{G} \ \mathtt{W} \ \mathtt{G} \ \mathtt{I} \ \mathtt{A} \ \mathtt{L} \ \mathtt{L} \ \mathtt{V} \ \mathtt{L} \ \mathtt{V} \ \mathtt{L} \ \mathtt{V} \ \mathtt{L} \ \mathtt{A} \ \mathtt{I} \ \mathtt{V} \ \mathtt{Y} \ \mathtt{L} \ \mathtt{I} \ \mathtt{A} \ \mathtt{L}$

AGCGGAGCCGGAGTGCCTGGCCTGGGCATTGCCCTCCTGGTCCTGGTCTGCGTCCTGGTCGCCATTGTGTATCTGATTGCCCTC

: MUC1R Gene Segment# : 16 : 226 Offset 1st Codon : 1

V C V L V A L A I V Y L I A L A V C Q C R R K N Y G Q L D I

: MUC1R Gene Segment# : 17 : 241 Offset

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1st Codon : 1

A V C Q C R R K N Y G Q L D I F P A R D T Y H P M S E Y P T GCCGTCTGCCAATGCAGAAGGAAAAACTATGGCCAACTGGATATCTTTCCCGCTAGGGATACCTATCACCCTATGTCCGAGTATCCCACA

Gene : MUC1R
Segment# : 18
Offset : 256
1st Codon : 1

Gene : MUC1R
Segment# : 19
Offset : 271
1st Codon : 1

Y H T H G R Y V P P S S T D R S P Y E K V S A G N G G S S L TACCATACCCATGGCAGATACGTCCCCCTAGGTCCCCCTATGAGAAAGTGTCCGCCGGAAACGGAGGCTCCAGCCTC

Gene : MUC1R
Segment# : 20
Offset : 286
1st Codon : 1

S P Y E K V S A G N G G S S L S Y T N P A V A A A S A N L A AGCCCTTACGAAAAGGTCAGCGCAATGGGCGAAGCTCCCTGTCCTACACAAACCCTGCCGTTGCCTTCCTCCGCCAATCTGGCT

Gene : MUC1R
Segment# : 21
Offset : 301
1st Codon : 1

S Y T N P A V A A A S A N L A A AGCTATACCAATCCCGCTGTGGCTGCCGCTAGCGCTAACCTCGCCGCT

Segments in scrambled order:

gp100 #4

W N R Q L Y P E W T E A Q R L D C W R G G Q V S L K V S N D TGGAATAGGCAACTGTATCCCGAATGGACAGGCTCAACGAT

TRP2 #6

Tyros #30

R N G D F F I S S K D L G Y D Y S Y L Q D S D P D S F Q D Y AGGAATGGCGATTTCTTTATCTCCAGCAAGACCTCGGCTATGACTATCTGCAAGACTCCGACCCTGACTCCTACAGACTAT

TRP-1 #1

A A P A F L T W H R Y H L L R L E K D M Q E M L Q E P S F S GCCGCTCCCGCTTTCCTCACCTGGCACAGATACCATCTGCTCAGGCTCGAGAAAGACATGCAGGAAATGCTCCAGGAACCCTCCTTCTCC

Tyros #29

G H N R E S Y M V P F I P L Y R N G D F F I S S K D L G Y D GGCCATAACAGAGAGTCCTACATGGTGCCTTTCATTCCCTCTACAGAAACGGAGACTTTTTCATTAGCTCCAAGGATCTGGGATACGAT

TRP2 #16

L L C L E R D L Q R L I G N E S F A L P Y W N F A T G R N E CTGCTCTGCCTCGAGAGAGAGACCAAAACGAA

gp100 #23

T T E V V G T T P G Q A P T A E P S G T T S V Q V P T T E V ACCACAGAGGTCGTGGGAACCCACACAGAGGGTCCACAGAGGGTCCACAGAGGGTCCACAGAGGGTCCACAGAGGGTC

MUCLR #9

S T D Y Y Q E L Q R D I S E M F L Q I Y K Q G G F L G L S N AGCACAGACTATTACCAAGAGCTCCAGAGAGACATTAGCGAAATCTTTCTGCAAATCTATAAGCAAGGCGGATTCCTCGGCCTCAGCAAT

gp100 #36

A C M E I S S P G C Q P P A Q R L C Q P V L P S P A C Q L V GCCTGTATGGAAATCTCCAGCCTGGCTGCAACTGGTC

TRP2 #31

D Q L G Y S Y A I D L P V.S V E E T P G W P T T L L V V M G

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GACCAACTGGGATACTCCTACGCTATCGATCTGCCTGTGTCCGTGGAAGAGACACCCCGGATGGCCTACCACACTGCTCGTGGTCATGGGA

TRP-1 #7

T E D G P I R R N P A G N V A R P M V Q R L P E P Q D V A Q ACCGAAGACGCATTAGGAGAAACCCTGCCGGAAACGTCGCCAGACCCAAGACGTCGCCCAAGACCCCAAGACGTCGCCCAAGACGTCGCCCAA

TRP2 #3

MUC1R #13

N Q Y K T E A A S R Y N L T I S D V S V S D V P F P F S A Q AACCAATACAAAACCGAAGCCGCTAGCAGATACAAATCTGACAATCTCCGACGTCAGCGTCAGCGATGTGCCTTTCCCTTTCTCCGCCCAA

TRP2 #1

A A M S P L W W G F L L S C L G C K I L P G A Q G Q F P R V GCCGCTATGTCCCCCGGTGGGGCTTTCTGCTCAGCTGTCTGGGATGCAAAATCCTCCCCGGAGCCCAAGGCCAATTCCCTAGGGTC

ap100 #18

gp100 #27

L A E M S T P E A T G M T P A E V S I V V L S G T T A A Q V CTGGCTGAGATGAGCACACAGCCACAGGCAGCTCAGGTC

MUCIR #13

MUC1F #7

MC1R #16

MCIR #20

L A L I I C N A I I D P L I Y A F H S Q E L R R T L K E V L CTGGCTCTGATTATCTGTAACGCTATCATTGACCCTCTGATTTACGCTTTCCATAGCCAAGAGCTCAGGAGAACCCTCAAGGAAGTGCTC

TRP2 #7

TRP2 #23

LS LQKFDNPPFFQNSTFSFRNALEGFDKADCTGTGCCTGCAAAAGGTTTGACAAAGCCTTTCTTTCAGAATAGCACATTCTCCTTCAGAAACGCTCTGGAAGGCTTTGACAAAGCCGAT

MUC1R #4

MUC1R #1

TRP2 #21

MUC1R #6

MC1R #13

F I A Y Y D H V A V L L C L V V F F L A M L V L M A V L Y V TTCATTGCCTATTACGATCACGTCGCCGTCCTCCTCGCCTCGTGGTCTTCTTCTTGGCTATGCTCGTCGTCGTGCTCTACGTC

Tyros #16

K L T G D E N F T I P Y W D W R D A E K C D I C T D E Y M G

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AAGCTCACCGGAGACGAAAACTTTACCATTCCCTATTGGGATTGGAGAGACGCTGAGAAATGCGATATCTGTACCGATGAGTATATGGGA

gp100 #32

L R L V K R Q V P L D C V L Y R Y G S F S V T L D I V Q G I CTGAGACTGGTCAAGAGACACTGTGTGCAAGGCATT

MUC1R #10

F L Q I Y K Q G G F L G L S N I K F R P G S V V V Q L T L A TTCCTCCAGATTACAAACAGGGAGGCTTTCTGGGACTGTCCAACATTAAGTTTAGGCCTGGCTCCGTGGTCGTGCAACTGACACTGGCT

MC1R #9

V I D V I T C S S M L S S L C F L G A I A V D R Y I S I F Y GTGATTGACGTCATCACATGCTCCAGCATGCTGTCTACTTCTAT

Tyros #21

TRP-1 #14

gp100 #39

V S L A D T N S L A V V S T Q L I M P G Q E A G L G Q V P L GGTCCCTGGCTGACACACACACACACACTCATCATGCCCGGACAGGAAGCCGGACTGGGACAGGTCCCCCTC

gp100 #20

G P V T A Q V V L Q A A I P L T S C G S S P V P G T T D G H GGCCCTGTGACAGCCCAAGTGGTCCTGCAAGCCGCTTGACAAGCTGTGGCTCCAGCCCTGTGCCTGGCACAACCGATGGCCAT

Tyros #8

qp100 #13

L G T H T M E V T V Y H R R G S R S Y V P L A H S S S A F T CTGGGAACCCATACCATGGGGTCTACCATAGGAGAGGCTCCAGGTCCTACGTCCCCTCGCCCATAGCTCCAGCGCTTTCACA

MC1R #12

A V A A I W V A S V V F S T L F I A Y Y D H V A V L L C L V GCCGTCGCCGCTATCTGGGTCGCTGGTCTGTTTTAGCACACTGTTTATCGCTTACTATGACCATGTGGCTGTGCTCCTGTGTCTGGTC

TRP2 #25

G T L D S Q V M S L H N L V H S F L N G T N A L P H S A A N GGCACACTGGATAGCCAAGTGATGAGCCTCCACAAATCTGGTCCACTCCTCCTCAACGGAACCAATGCCCTCCCCCATAGCGCTGCCAAT

MART #4

Tyros #15

PWHRLFLLRWEQEIQKLTGGDENFTIPYWDWCCCTGGCACAGACTGTTTCTGCTCAGGTGGGAGCAAGAGATCAGAAACTGACAGGCGATGAGAATTCACAATCCCTTACTGGGACTGG

MC1R #1

A A M A V Q G S Q R R L L G S L N S T P T A I P Q L G L A A GCCGCTATGGCTGCAAGGCTCCAGGAAAGGCTCCAAGCTCCAACTCCACCCTACCGCTATCCCTCAGCTCGGCCTCGCCGCT

MC1R #F

VVATIAKNRNLHSPMYCFICCLALSDLLVS GTGGTCGCCACAATCGCAAAGAATCGCATAGCCCTATGTATTGCTTTATCTGTTGCCCTCAGCGATCTGCTCGTGTCC

Tyros #25

Q S S M H N A L H I Y M N G T M S Q V Q G S A N D P I F L L CAGTCCAGCATGCACCATTTACATGAACGGAACCATGAGCCAAGTGCAAGGCTCCGCCAATGACCCTATCTTCTGCTC

Tyros #18

f G Q H P T N P N L L S P A S F F S S W Q I V C S R L E E Y N GGCCAACACCCTACCAATCCCAATCTGCTCCAGCCCTGCCTCCTTCTTTAGCTCCTGGCAAATCGTCTGCTCCAGGCTCGAGGAATACAAT

MCIR #6

Y C F I C C L A L S D L L V S G T N V L E T A V I L L E A

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TRP2 #19

D P T L I S R N S R F S S W E T V C D S L D D Y N H L V T L GACCCTACCCTCATCTCCAGGAATAGCAGATTCTCCAGCTGGGAGACAGTGTGTGACTCCCTGGATGACTATAACCATCTGGTCACCCTC

TRPALGSTTPPAHDVTSAPDNKAA ${\tt ACCAGACCCGCTCTGGGAAGCACAACCCCTCCCGCTCACGATGTGACAAGCGCTCCCGATAACAAAGCCGCT}$

Tyros #17

R D A E K C D I C T D E Y M G G Q H P T N P N L L S P A S F $\tt AGGGATGCCGAAAAGTGTGACATTTGCACAGACGAATACATGGGCGGACAGCATCCCACAAACCCTAACCTCCTGTCCCCGCTAGCTTT$

gp100 #17
T F A L Q L H D P S G Y L A E A D L S Y T W D F G D S S G T

S S A D V E F C L S L T Q Y E S G S M D K A A N F S F R N T AGCTCCGCCGATGTGGAATTCTGTCTGTCCCTGACACAGTATGAGTCCGGCTCCATGGATAAGGCTGCCAATTTCTCCTTCAGAAACACA

ap100 #6

G P T L I G A N A S F S I A L N F P G S Q K V L P D G Q V I $\overline{\tt GGCCCTACCCTCATCGGAGCCAATGCCTCCTTCTCCATCGCTCTGAATTTCCCTGGCTCCCAGAAAGTGCTCCCCGATGGCCAAGTGATT$

WGPFFLHLTLIVLCPEHPTCGCIFKNFNLF ${\tt TGGGGACCCTTTTTCCTCCACCTCACCTCATCGTCCTGTGTCCCGAACACCCTTACCTGTGGCTGTATCTTTAAGAATTTCAATCTGTTT}$

C Q C S G N F M G F N C G N C K F G F W G P N C T E R R L L $\tt TGCCAATGCTCCGGCAATTTCATGGGCTTTAACTGTGGCAATTGCAAATTCGGATTCTGGGGCCCTAACTGTACCGAAAGGAGACTGCTC$

Q Y R R L R K G Y T P L M E T H L S S K R Y T E E A A A CAGTATAGGAGACTGAGAAAGGGATACACACCCCTCATGGAAACCCATCTGTCCAGCAAAAGGTATACCGAAGAGGCTGCCGCT

P L E N A P I G H N R Q Y N M V P F W P P V T N T E M F V T CCCCTCGAGAATGCCCCTATCGGACACAATAGGCAATACAATATGGTCCCCTTTTGGCCTCCCGTCACCAATACCGAAATGTTTGTGACA

ap100 #7

N F P G S Q K V L P D G Q V I W V N N T I I N G S Q V W G G

R P T A E A P N T T A G Q V P T T E V V G T T P G Q A P T A AGGCCTACCGCTGAGGCTCCCAATACCACAGCCGGACAGGTCCCCACAACCGAAGTGGTCGGCACAACCCCTGGCCAAGCCCCTACCGCT

STPGGEKETSATQRSSVPSSTEKNAVSMTS AGCACACCGGGAGGCGAAAAGGAAACCTCCGCCACACAGAGAAGCTCCGTGCCTAGCTCCACCGAAAAGAATGCCGTCAGCATGACCTCC

LIYRRRLMKQDFSVPQLPHSSSHWLRLPRI $\tt CTGATTTACAGAAGGAGACTGATGAAGCAAGACTTTAGCGTCCCCCAACTGCCTCACTCCAGCTCCCACTGGCTGAGACTGCCTAGGATT$

LGLLGPNGTQPQFANCSVYDFFVWLHYYSV $\tt CTGGGACTGCTCGGCCCTAACGGAACCCCAATTCGCTAACTGTAGCGTCTACGATTTCTTTGTGTGGCTGCATTACTATAGCGTC$

TRP-1 #9

C L E V G L F D T P P F Y S N S T N S F R N T V E G Y S D P

A A M D L V L K R C L L H L A V I G A L L A V G A T K V P R ${\tt GCCGCTATGGATCTGGTCCTGAAAAGGTGTCTGCTCCACCTCGCCGTCATCGGAGCCCTCCTGGCTGTGGGAGCCACAAAGGTCCCCAGA}$

MC1R #3

N Q T G A R C L E V S I S D G L F L S L G L V S L V E N A L

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Tyros #23

S G S M D K A A N F S F R N T L E G F A S P L T G I A D A S AGCGGAAGCATGGACAAGCCTTTAGCTTTAGGAATACCCTCGAGGGATTCGCTAGCCTCTGACAGGCATTGCCGATGCCTCC

Tyros #4

S P C G Q L S G R G S C Q N I L L S N A P L G P Q F P F T G AGCCCTTGCGGACAGCTCAGCTGCGGAAGGGGAAGGTGCAGAATATCCTCCTGTCCAACGCTCCCCTCGGCCCTCAGTTTCCCTTTACCGGA

Tyros #13

M H Y Y V S M D A L L G G S E I W R D I D F A H E A P A F L ATGCATTACTATGTGTCCATGGATGCCCTCCTGGGAGGCTCCGGAGATTTGGAGAGACATTGACTTTGCCCATGAGGCTCCCGCTTTCCTC

Tyros #35

E E K Q P L L M E K E D Y H S L Y Q S H L A A GAGGAAAAGCAACCCCTCCTGATGGAGAAAGGATTACCATAGCCTCTACCAAAGCCATCTGGCTGCC

TRP2 #5

G Q C T E V R A D T R P W S G P Y I L R N Q D D R E L W P R GGCCAATGCACAGAGGTCAGGGCTGACACAAGGCCTTGGTCCGGCCCTTACATTCTGAGAAACCAAGACGATAGGGAACTGTGGCCCAGA

MUC1F #4

S V P S S T E K N A V S M T S S V L S S H S P G S G S S T T AGCGTCCCTCCAGCACAGAGAAAAAACGCTGTGTCCATGACAAGCTCCGTGCTCAGCTCCCACTCCCCGGAAGCGGAAGCTCCACCACA

Tyros #12

T P M F N D I N I Y D L F V W M H Y Y V S M D A L L G G S E ACCCCTATGTTTAACGATATCAATATCTATGACCTCTTCGTCTGGATGCACTATTACGTCAGCATGGACGCTCTGCTCGGCGGAAGCGAA

ap100 #9

Q P V Y P Q E T D D A C I F P D G G P C P S G S W S Q K R S CAGCCTGTGTATCCCCAAGAGACAGACGATGCCTGTATCTTTCCCGATGGCGGACCCTGTCCCTCCGGCTCCTGGTCCCAGAAAAGGTCC

TRP-1 #6

D S L E D Y D T L G T L C N S T E D G P I R R N P A G N V A GACTCCCTGGAAGACTATGACACACTGGGAACCCTCTGCAATAGCACAGAGGATGGCCCTATCAGAAGGAATCCCGCTGGCAATGTGGCT

mo100 #8

W V N N T I I N G S Q V W G G Q P V Y P Q E T D D A C I F P TGGGTCAACAATACCATTATCAATGGCTCCAGGTCTGGGGAGGCCAACCCGTCTACCCTCAGGAAACCGATGACGCTTGCATTTTCCCT

MART #7

gp100 #14

SRSYVPLAHSSSAFTITDQVPFSVSVSQLR AGCAGAAGCTATGTGCCTCTGGCTCACCTCCGCCTTTACCGTTACCGATCAGGTCCCCTTTAGCGTCAGCGTCAGCCAACTGAGA

TRP-1 #2

TRP-1 #16

TRP2 #13

C S V Y D F F V W L H Y Y S V R D T L L G P G R P Y R A I D
TGCTCCGTGTATGACTTTTTCGTCTGGCTCCACTATTACTCCGTGAGAGACACTGCTCGGCCCTGGCAGACCCTATAGGGCTATCGAT

Tyros #9

MART #2

K K G H G H S Y T T A E E A A G I G I L T V I L G V L L L I AAGAAAGGCCATGGCCATACCACAGCCGAAGAGGCCTGCCGGAATCGGAATCCTCACCGTCATCCTCGGCGTCCTCCTGATT

gp100 #11

F V Y V W K T W G Q Y W Q V L G G P V S G L S I G T G R A M

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 ${\tt TTCGTCTACGTCTGGAAAACCTGGGGCCAATACTGGCAGGTCCTGGGAGGCCCTGTGTCCGGCCTCAGCATTGGCACAGGCCAGGCCATGGCCAGGCAGGCCAGGCCAGGCCAGGCCAGGCCAGGCCAGGCCAGGCCAGGCCAGGCCAGGCCAGGCCAGGCCAGGCCAGGCCAGGCCAGGCCAGGCCCAGGCCAGGCCAGGCCAGGCCAGGCCAGGCCAGGCCAGG$

gp100 #12

gp100 #25

Tyros #19

FSSWQIVCSRLEEYNSHQSLCNGTTPEGPLRTTCTCCAGCTGGCAGTTGTGTGTGGCAGCTGGAAGGCCTCTGAAGCCTCTGCAATGGCACCCCCAAGGCCCTCTGAGA

TRP2 #27

D P I F V V L H S F T D A I F D E W M K R F N P P A D A W P GACCCTATCTTTGTGGTCCTGCATAGCTTTACCGATGCCATTTCGATGAGTGAAAAGGTTTAACCCTCCCGCTGACGCTTGGCCT

MClR #15

H M L A R A C Q H A Q G I A R L H K R Q R P V H Q G F G L K CACATGCTGGCTAGGGCTTGCAACACGCTCAGGGAATCGCTAGGCTCCACAAAAGGCCAAAAGGCCTGTGCATCAGGGATTCGGACTGAAA

MUC1F #2

gp100 #44

F C S C P I G E N S P L L S G Q Q V A A
TTCTGTAGCTGTCCCATTGGCGAAAACTCCCCCCTCCTGTCCGGCCAACAGGTCGCCGCT

TRP2 #24

T F S F R N A L E G F D K A D G T L D S Q V M S L H N L V H ACCTTTAGCTTTAGGAATGCCCTCGAGGGATTCGATAAGGCTGACGGAACCCTCGACTCCAGGTCATGTCCCTGCATAACCTCGTGCAT

Tyros #20

S H Q S L C N G T P E G P L R R N P G N H D K S R T P R L P AGCCATCAGTCCCTGTGTAACGGAACCCCTGAGGGACCCCTCAGGAGAAACCCTGGCAATCACGATAAGTCCAGGACACCCAGACTGCCT

TRP2 #30

PFFPPVTNEELFLTSDQLGYSYAIDLPVSVCCCTTTTTCCCTCCCGTCACCAATGAGGAACTGTTTCTGACAAGCGATCAGCTCGGCTATAGCTATGCCATTGACCTCCCCGTCAGCGTC

TRP2 #9

TRP2 #29

gp100 #28

MUCIR #7

T S P Q L S T G V S F F F L S F H I S N L Q F N S S L E D P ACCTCCCCCCAACTGTCCACCGGAGTGTCCTTCTTTTTCCTCAGCTTTCACATTAGCAATCTGCAATTCAATAGCTCCCTGGAAGACCCT

MUC1R #19

YHTHGRYVPPSSTDRSPYEKVSAGNGGSSL TACCATACCCATGGCAGATACGTCCCCCTAGCTCCACCGATAGGTCCCCCTATGAGAAAGTGTCCGCCGGAAACGGAGGCTCCAGCCTC

MClR #4

L F L S L G L V S L V E N A L V V A T I A K N R N L H S P M CTGTTTCTGTCCCTGGGACTCGTCAGAAAACGCTCCACTCCCCCATG

TRP2 #26

MUC1R #17

AVCQCRRKNYGQLDIFPARDTYHPMSEYPT

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MC1R #14

V F F L A M L V L M A V L Y V H M L A R A C Q H A Q G I A R GTGTTTTTCCTCGCCATGCTGGTCCTGATGGCCGTCCTGTATGTGCCATGCCAGAGCCTGTCAGCATGCCCAAGGCATTGCCAGA

TRP-1 #10

S T N S F R N T V E G Y S D P T G K Y D P A V R S L H N L A AGCACAAACTCCTTCAGAAACACAGTGGAAGGCTATAGCGATCCCACAGGCAAATACGATCCCGCTGTGAGAAGCCTCCACAATCTGGCT

TRP-1 #3

L P Y W N F A T G K N V C D I C T D D L M G S R S N F D S T CTGCCTTACTGGAACTTTGCCACAGGCAAAAACGTCTGCGATATCTGTACCGATGACCTCATGGGAAGCAGAAGCAATTTCGATAGCACA

ap100 #15

MUC1R #8

F H I S N L Q F N S S L E D P S T D Y Y Q E L Q R D I S E M TTCCATATCTCCAACCTCCAGCTTTAACTCCCAGCCTCGAGGATCCCTCCACCGATTACTATCAGGAACTGCAAAGGGATATCTCCGAGATG

MUC1R #20

S P Y E K V S A G N G G S S L S Y T N P A V A A A S A N L A AGCCCTTACGAAAAGGTCAGCGCTGGCAATCTGGCT

Tyros #11

Y V I P I G T Y G Q M K N G S T P M F N D I N I Y D L F V W TACGTCATCCCTATCGGAACCTATGGCCAAATGAAAAACGGAAGCACCCATGTTCAATGACATTAACATTTACGATCTGTTGTGTGG

gp100 #37

ap100 #33

R Y G S F S V T L D I V Q G I E S A E I L Q A V P S G E G D AGGTATGGCTCCTTCCGTGACACTGGATATCGTCCAGGGAATCGAAGCGCTGAGATTCTGCAAGCCGTCCCTCCGGCGAAGGCGAT

Tyros #27

H H A F V D S I F E Q W L Q R H R P L Q E V Y P E A N A P I CACCATGCCTTTGTGGATAGCATTTTCGAACAGTGGCTGCAAAGGCATAGGCCTCTGCAAGAGGTCTACCCTGAGGCTAACGCTCCCATT

TRP-1 #4

C T D D L M G S R S N F D S T L I S P N S V F S Q W R V V C TGCACAGACGATCTGATGGGTCCAACTTTGACTCCACCTCATCTCCCCCAATAGCGTCTTCTCCCCAGTGGAGGGTCGTGTGT

MUCLR #18

MUC1R #21

S Y T N P A V A A A S A N L A A AGCTATACCAATCCCGCTGTGGCTGCCGCTAGCGCTAACCTCGCCGCT

MC1R #19

E H P T C G C I F K N F N L F L A L I I C N A I I D P L I Y GAGCATCCCACATGCGATGCCATTATCGAAAACTTTAACCTCTTCCTCGCCCTCATCATTTGCAATGCCATTATCGATCCCCTCATCTAT

Tyros #26

MSQVQGSANDPIFLLHHAFVDSIFEQWLQR ATGTCCCAGGTCCAGGGAAGCGCTAACGATCCCATTTTCCTCCTGCATCACGCTTTCGTCGACTCCATCTTTGAGCAATGGCTCCAGAGA

TRP2 #22

gp100 #19

LISRALVVTHTYLEPGPVTAQVVLQAAIPL CTGATTAGCAGAGCCCTCGTGGTCACCCATACCTATCTGGAACCCGGACCCGTCACCGTCAGGTCGTGCTCCAGGCTGCCATTCCCCTC

TRP2 #17

S F A L P Y W N F A T G R N E C D V C T D Q L F G A A R P D

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gp100 #2

V I G A L L A V G A T K V P R N Q D W L G V S R Q L R T K A GTGATTGGCGCTCTGCTCGCCGTCGGCGCTACCAAAGTGCCTAGGAATCAGGATTGGCTCGGCGTCAGCAGACAGCACAAAGTGCT

gp100 #16

À L D G G N K H F L R N Q P L T F A L Q L H D P S G Y L A E GCCCTCGACGGAGGCAATAAGCATTCCTCAGGAATCAGCCTCTGACATTCGCTCTGCAACTGCATGACCCTAGCGGATACCTCGCCGAA

TRP2 #18

C D V C T D Q L F G A A R P D D P T L I S R N S R F S S W E TGCGATGTGTGTGCCGATCAGCTCTTCGGAGCCGCTAGGCCTGACGATCCCACACTGATTAGCAGAAACTCCAGGTTTAGCTCCTGGGAA

MART #3

A A M P R E D A H F I Y G Y P K K G H G H S Y T T A E E A A GCCGCTATGCCTAGGGAAGAGCGCTCACTTATCTATGGCTATCCCAAAAAGGGACACCGCTACACAACCGCTGAGGAAGCCGCT

TRP-1 #11

MUC1R #14

S D V S V S D V P F P F S A Q S G A G V P G W G I A L L V L AGCGATGTGCCGTGTCCGTCTTCCCTTTAGCGCTCAGTCCGGCGCTGGCGTCCCCGGATGGGGAATCGCTCTGCTCTGCTCT

TRP2 #10

S P Q E R E Q F L G A L D L A K K R V H P D Y V I T T Q H W AGCCCTCAGGAAAGGGAACAGTTTCTGGGAGCCCTCGACCTCGCCAAAAGGAGAGTGCATCCCGATTACGTCATCACAACCCAACACTGG

Tyros #10

F F A Y L T L A K H T I S S D Y V I P I G T Y G Q M K N G S TTCTTTGCCTATCTGACACTGGCTAAGCATACCATTAGCTCCGACTATGTGATTCCCATTGGCACATACGGACAGATGAAGAATGGCTCC

MC1R #7

G T N V L E T A V I L L E A G A L V A R A A V L Q Q L D N GGCACAAACGTCCTGGAAACGCTCGTGATTCTGCTCCTGGAAGCCGGAGCCCTCGTGGCTAGGGCTGCCGTCCTGCAACAGCTCGACAAT

MUC1R #16

V C V L V A L A I V Y L I A L A V C Q C R R K N Y G Q L D I GTGTGTGTGTGTGTGTGTGTGTGTGGGAGAAGAATTACGGACAGCTCGACATT

MART #6

C P Q E G F D H R D S K V S L Q E K N C E P V V P N A P P A TGCCCTCAGGAAGGCTTTGACCATAGGGATAGCAAAGTGTCCCTGCAAGAGAAAAACTGTGAGCCTGTGGTCCCCAATGCCCTCCCGCT

MUC1F #5

TRP2 #28

D E W M K R F N P P A D A W P Q E L A P I G H N R M Y N M V GACGAATGGATGAAGAGTTCAATCCCCCTGCCGATGCCCCAAGAGCTCGCCCTATCGGACACAATAGGATGTACAATATGGTC

MC1R #23

A F H S Q E L R R T L K E V L T C S W A A GCCTTTCACTCCCAGGAACTGAGAAGGACACTGAAAGAGGTCCTGACATGCTCCTGGGCTGCC

TRP2 #15

F S H Q G P A F V T W H R Y H L L C L E R D L Q R L I G N E TTCTCCCACCAAGGCCCTTCTGTGACATGGCATAGGTATCACCTCCTGTGTCTGGAAAGGGATCTGCAAAGGCTCATCGGAAACGAA

TRP-1 #8

R P M V Q R L P E P Q D V A Q C L E V G L F D T P P F Y S N AGGCCTATGGTCCAGAGACTGCCTGAGCCTCAGGATGTGGCTCTGGAAGTGGGACTGTTTGACACACCCCCTTTCTATAGCAAT

TRP-1 #13

Q D P I F V L L H T F T D A V F D E W L R R Y N A D I S T F CAGGATCCCATTTCGTCCTGCTCCACCATTCACAGACGCTGTGTTTGACGAATGGCTCAGGAGATACAATGCCGATATCTCCACCTTT

TRP2 #4

LGAESANVCGSQQGRGQCTEVRADTRPWSG

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TRP2 #8

TRP-1 #12

H L F L N G T G G Q T H L S S Q D P I F V L L H T F T D A V CACCTCTTCCTCAACGGAACCGGAGGCCAAACCCATCTGTCCAGCCAAGACCCTATCTTTGTGCTCCTGCATACCTTTACCGATGCCGTC

Tyros #34

G L V S L L C R H K R K Q L P E E K Q P L L M E K E D Y H S GGCCTCGTGTCCTGCTGCTGCAAAAGGAAAAGGAAACAGCTCCCCGAAGAAAACAGCCTCTGCTCATGGAAAAGGAAAAGAACATATCACTCC

TRP2 #2

G C K I L P G A Q G Q F P R V C M T V D S L V N K E C $ilde{C}$ P R GGCTGTAAGATTCTGCCTGGCGTCAAGAGATGCTGTCCCAGA

gp100 #43

qp100 #10

D G G P C P S G S W S Q K R S F V Y V W K T W G Q Y W Q V L GACGGAGGCCCTTGCCCTAGCGGAAGCTGGAGCCCAAAAGAGAAGCTTTGTGTATGTGTGGAAGACATGGGGACAGTATTGGCAAGTGCTC

gp100 #3

N Q D W L G V S R Q L R T K A W N R Q L Y P E W T E A Q R L AACCAAGACTGGCTGGGAGCTGGAACAGCTCTACCCTGAGTGGACCGAAGCCCAAAGGCTC

Tyros #14

I W R D I D F A H E A P A F L P W H R L F L L R W E Q E I Q ATCTGGAGGGATATCGATTCGCTCACGAAGCCCCTGCCTTCTGCCTTGGCATAGGCTCTTCCTCCTGAGATGGGAACAGGAAATCCAA

MIICTE #1

A A M T P G T Q S P F F L L L L T V L T V V T G S G H A S GCCGCTATGACACCCGGAACCCAAAGCCCTTTCTTCTGCTCCTGCTCCTGACAGTGCTCACCGTCGTGACAGGCTCCGGCCATGCCTCC

ART HS

D K S L H V G T Q C A L T R R C P Q E G F D H R D S K V S L GACAAAAGCCTCCACGTCGCCACAGAGGTCTCCCCAAGAGGGATTCGATCACAGAGACTCCAAGGTCAGCCTC

MUC1R #2

N V T S A S G S A S G S A S T L V H N G T S A R A T T T P A AACGTCACCTCCGCCTCCGCCTCCGCCTCCGCCTCCGCCTCCGCCTCCGCCACACCACCCCCCT

Tyros #24

LEGFASPLTGIADASQSSMHNALHIYMNGTCTGGAAGGCTTTGCCTCCCCCCTCACCGGAATCGCTGACGCTAGCCAAAGCTCCATGCATAACGCTCTGCATATCTATATGAATGGCACA

TRP2 #14

Tyros #1

A A M L L A V L Y C L L W S F Q T S A G H F P R A C V S S K GCCGCTATGCTCCTGCTCTGCTCTGGTCCTCCGCCGGACACCTTTCCCAGAGCCTGTGTGTCCAGCAAA

an100 #35

A F E L T V S C Q G G L P K E A C M E I S S P G C Q P P A Q GCCTTTGAGCTCACCGTCAGCTGTCAGGGAGGCCTCCCCAAAGAGGCTTGCATGGAGATTAGCTCCCCGGATGCCAACCCCCTGCCCAA

Tyros #6

V D D R E S W P S V F Y N R T C Q C S G N F M G F N C G N C GTGGATGACAGAGAGTCCTGGCCTAGCGTCTTCTATAACAGAACCTGTCAGTGTAGCGGAAACTTTATGGGATTCAATTGCGGAAACTGT

gp100 #34

TRP2 #20

TVCDSLDDYNHLVTLCNGTYEGLLRRNQMG

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Tyros #5

L L S N A P L G P Q F P F T G V D D R E S W P S V F Y N R T CTGCTCAGCAATGCCCTCTGGGACCCCAATTCCCTTTCACAGGCGTCGACAATAGGAAAGCTGGCCTCCGTGTTTTACAATAGGACA

MART #8

Y E K L S A E Q S P P P Y S P A A TACGAAAAGCTCAGCGCTGAGCAAAGCCCTCCCCTTACTCCCCCGCTGCC

gp100 #41

I V G I L L V L M A V V L A S L I Y R R R L M K Q D F S V P ATCGTCGGCATCTGGTCGTCGTCGTCGTCGTCGCTGCCTTGCTATGGAAACAGGATTTCTCCGTGCCT

MART #3

Tyros #31

MUC1F #6

Q G Q D V T L A P A T E P A S G S A A T W G Q D V T S V P V CAGGGACAGGATGTGACACTGCTCCCGCTACCGAACCCGCTAGCGGAAGCGCTCCCACATGGGGACAGGATGTGACAAGCGTCCCCGTC

gp100 #21

MUC1R #3

L V H N G T S A R A T T T P A S K S T P F S I P S H H S D T CTGGTCCACAATGGCACAAGCGCTAGGGCTACCACAACCCCTGCCTCCAAGTCCACCCCTTTCTCCATCCCTAGCCATCACTCCGACACA

TRP2 #32

E E T P G W P T T L L V V M G T L V A L V G L F V L L A F L GAGGAAACCCTGGCTGGCCCACAACCCTCCTGGTCGTCATGGGCACACTGGTCGCCCTCGTGGGACTGTTTGTGCTCCTGGCTTTCCTC

gp100 #29

T T T E W V E T T A R E L P I P E P E G P D A S S I M S T E ACCACAACCGAATGGGTCGAGAACCGCTAGGGAACTGCCTATCCCTGAGCCTGAGGGACCCGATGCCTCCAGCATTATGTCCACCGAA

MC1R #17

Tyros #33

L G A A M V G A V L T A L L A G L V S L L C R H K R K Q L P CTGGGAGCCGCTATGGTCGGCGCTCTGCTCACCGCTCTGCTCGCCGGACTGGTCAGCCTCCTGTGTAGGCATAAGAGAAAGCAACTGCCT

MClR #8

G A L V A R A A V L Q Q L D N V I D V I T C S S M L S S L C GGCGCTCTGGTCGCCAGAGCCGCTGCTCCAGCAACTGGATAACGTCATCGATGTGATTACCTGTAGCTCCATGCTCAGCTCCCTGTGT

gp100 #26

M T P E K V P V S E V M G T T L A E M S T P E A T G M T P A ATGACACCCGGAAAAGGTCCCCGTCAGCGAAGTGATGACCCGCTAACCCCCTGAGGCTACCCGGAATGACACCCGCT

Tvros #2

Q T S A G H F P R A C V S S K N L M E K E C C P P W S G D R CAGACAAGCGCTGGCCATTCCCTAGGGCTTGCGTCAGCTCCAAGAATCTGATGGAGAAAGAGTGTTGCCCTCCTGGAGCGGAGACAGA

MC1R #13

A L R Y H S I V T L P R A P R A V A A I W V A S V V F S T L GCCCTCAGGTATCACCTCCATCGTCACCCTCCCAGAGCCCCTAGGGCTGTGCCTTTTGGGTCGCCTCCGTGGTCTTCTCCACCCTC

MUC1R #12

FREGTINVHDVETQFNQYKTEAASRYNLTI

Tyros #3

NL M E K E C C P P W S G D R S P C G Q L S G R G S C Q N I

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 $\verb|AACCTCATGGAAAAGGAATGCTGTCCCCCTTGGTCCGGCGATAGGTCCCCCTGTGGCCAACTGTCCGGCAGAGGCTCCTGCCAAAACATT$

I K S Y L E Q A S R I W S W L L G A A M V G A V L T A L L A

PTTLASHSTKTDASSTHHSSVPPLTSSNHS $\tt CCCACAACCCTCGCCTCCACCACCAAAACCGATGCCTCCAGCACACCACACCATAGCTCCGTGCCTCCACCTCCAGCAATCACTCC$

S G A G V P G W G I A L L V L V C V L V A L A I V Y L I A L AGCGGAGCCGGAGTGCCTGGCTGGGCATTGCCCTCCTGGTCCTGGTCTGCGTCCTGGTCGCCCTCGCCATTGTGTATCTGATTGCCCTC

F L G A I A V D R Y I S I F Y A L R Y H S I V T L P R A P R $\verb|TTCCTCGGCGCTATCGCTGTGGATAGGTATATCTCCATCTTTTACGCTCTGAGATACCATAGCATTGTGACACTGCCTAGGGCTCCCAGA$

gp100 #40 LIMPGQEAGLGQVPLIVGILLVLMAVVLAS

T L V A L V G L F V L L A F L Q Y R R L R K G Y T P L M E T ACCCTCGTGGCTCTGGTCGGCCTCTTCGTCCTGCTCGCCTTTCTGCAATACAGAAGGCTCAGGAAAGGCTATACCCCTCTGATGGAGACA

LISPNSVFSQWRVVCDSLEDYDTLGTLCNS CTGATTAGCCCTAACTCCGTGTTTAGCCAATGGAGAGTGGTCTGCGATAGCCTCGAGGATTACGATACCCTCGGCACACTGTGTAACTCC

L N S T F T A I P Q L G L A A N Q T G A R C L E V S I S D G

Tyros #28 HRPLQEVYPEANAPIGHNRESYMVPFIPLY ${\tt CACAGACCCTTCAGGAAGTGTATCCCGAAGCCAATGCCCCTATCGGACACAATAGGGAAAGCTATATGGTCCCTTTATCCCTCTGTAT}$

EPSGTTSVQVPTTEVISTAP.VQMPTAESTG GAGCCTAGCGGAACCACAAGCGTCCAGGTCCCCACAACCGAAGTGATTAGCACAGCCCCTGTGCAAATGCCTACCGCTGAGTCCACCGGA

K K R V H P D Y V I T T Q H W L G L L G P N G T Q P Q F A N AAGAAAAGGGTCCACCCTGACTATGTGATTACCACACAGCATTGGCTCGGCCTCCTGGGACCCAATGGCACAGCCTCAGTTTGCCAAT

LHQILKGGSGTYCLNVSLADTNSLAVVSTQ

gpl00 #30
PEPEGPDASSIMSTESITGSLGPLLDGTAT $\tt CCCGAACCCGAAGGCCCTGACGCTAGCTCCATCATGAGCACAGAGTCCATCACAGGCTCCCTGGGACCCCTCCTGGATGGCACAGCCACA$

S I T G S L G P L L D G T A T L R L V K R Q V P L D C V L Y AGCATTACCGGAAGCCTCGGCCCTCTGCTCGACGGAACCGCTACCCTCAGGCTCGTGAAAAGGCAAGTGCCTCTGGATTGCGTCCTGTAT

D C W R G G Q V S L K V S N D G P T L I G A N A S F S I A L GACTGTTGGAGAGGGGGACAGGTCAGCCTCAAGGTCAGCAATGACGGACCCACACTGATTGGCGCTAACGCTAGCTTTAGCATTGCCCTC

Synthetic Protein:

wnrqlypewteAQRldcwrggQvslkvsndpyilrnQddrelwprkffhrtckCtgnfagrngdffisskdlgydysylQdsdpdsfQdyaApafltw HRYHLLRLEKDMQEMLQEPSFSGHNRESYMVPF1PLYRNGDFF1SSKDLGYDLLCLERDLQRL1GNESFALPYWNFATGRNETTEVVGTTPGQAPTAE ${\tt PSGTTSVQVPTTEVSTDYYQELQRDISEMFLQIYKQGGFLGLSNACMEISSPGCQPPAQRLCQPVLPSPACQLVDQLGYSYAIDLPVSVEETPGWPTT}$ LLVVMGTEDGPIRRNPAGNVARPMVQRLPEPQDVAQCMTVDSLVNKECCPRLGAESANVCGSQQGRNQYKTEAASRYNLTISDVSVSDVPFPFSAQAA MSPLWWGFLLSCLGCKILPGAQGQFPRVADLSYTWDFGDSSGTLISRALVVTHTYLEPLAEMSTPEATGMTPAEVSIVVLSGTTAAQVIKFRPGSVVV QLTLAFREGTINVHDVETQFGSAATWGQDVTSVPVTRPALGSTTPPAHDVLHKRQRPVHQGFGLKGAVTLTILLGIFFLCLALIICNAIIDPLIYAFH SQELRRILKEVLKFFHRTCKCTGNFAGYNCGDCKFGWTGPNCLSLQKFDNPPFFQNSTFSFRNALEGFDKADSKSTPFSIPSHHSDTPTTLASHSTKT

DASSAANRPALGSTAPPVHNVTSASGSASGSASTCNGTYEGLLRRNQMGRNSMKLPTLKDIRDCTHHSSVPPLTSSNHSTSPOLSTGVSFFFLSFIAY

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YDHVAVLLCLVVFFLAMLVLMAVLYVKLTGDENFTIPYWDWRDAEKCDICTDEYMGLRLVKRQVPLDCVLYRYGSFSVTLDIVQGIFLQIYKQGGFLG LSNIKFRPGSVVVQLTLAVIDVITCSSMLSSLCFLGAIAVDRYISIFYRNPGNHDKSRTPRLPSSADVEFCLSLTQYEFDEWLRRYNADISTFPLENA PIGHNRQYNMVSLADTNSLAVVSTQLIMPGQEAGLGQVPLGPVTAQVVLQAAIPLTSCGSSPVPGTTDGHKFGFWGPNCTERRLLVRRNIFDLSAPEK DKLGTHTMEVTVYHRRG\$R\$YVPLAH\$\$\$AFTAVAAIWVA\$VVF\$TLFIAYYDHVAVLLCLVGTLD\$QVM\$LHNLVH\$FLNGTNALPH\$AANGCWYCR RRNGYRALMDKSLHVGTQCALTRRPWHRLFLLRWEQEIQKLTGDENFTIPYWDWAAMAVQGSQRRLLGSLNSTPTAIPQLGLAAVVATIAKNRNLHSP MYCFICCLALSDLLVSQSSMHNALHIYMNGTMSQVQGSANDPIFLLGQHPTNPNLLSPASFFSSWQIVCSRLEEYNYCFICCLALSDLLVSGTNVLET ${ t AVILLLEADPTLISRNSRFSSWETVCDSLDDYNHLVTLTRPALGSTTPPAHDVTSAPDNKAARDAEKCDICTDEYMGGQHPTNPNLLSPASFTFALQL$ $\verb|HDPSGYLAEADLSYTWDFGDSSGTSSADVEFCLSLTQYESGSMDKAANFSFRNTGPTLIGANASFSIALNFPGSQKVLPDGQVIWGPFFLHLTLIVLC$ PEHPTCGCIFKNFNLFCQCSGNFMGFNCGNCKFGFWGPNCTERRLLQYRRLRKGYTPLMETHLSSKRYTEEAAAPLENAPIGHNRQYNMVPFWPPVTN TEMFVTNFPGSQKVLPDGQVIWVNNTIINGSQVWGGRPTAEAPNTTAGQVPTTEVVGTTPGQAPTASTPGGEKETSATQRSSVPSSTEKNAVSMTSLI $\tt YRRRLMKQDFSVPQLPHSSSHWLRLPRILGLLGPNGTQPQFANCSVYDFFVWLHYYSVCLEVGLFDTPPFYSNSTNSFRNTVEGYSDPAAMDLVLKRC$ LLHLAVIGALLAVGATKVPRNQTGARCLEVSISDGLFLSLGLVSLVENALSGSMDKAANFSFRNTLEGFASPLTGIADASSPCGQLSGRGSCQNILLS NAPLGPQFPFTGMHYYVSMDALLGGSEIWRDIDFAHEAPAFLEEKQPLLMEKEDYHSLYQSHLAAGQCTEVRADTRPWSGPYILRNQDDRELWPRSVP SSTEKNAVSMTSSVLSSHSPGSGSSTTTPMFNDINIYDLFVWMHYYVSMDALLGGSEQPVYPQETDDACIFPDGGPCPSGSWSQKRSDSLEDYDTLGT LCNSTEDGPIRRNPAGNVAWVNNTIINGSQVWGGQPVYPQETDDACIFPQEKNCEPVVPNAPPAYEKLSAEQSPPPYSPSRSYVPLAHSSSAFTITDQ VPFSVSVSQLRLEKDMQEMLQEPSFSLPYWNFATGKNVCDIVPFWPPVTNTEMFVTAPDNLGYTYEAACSVYDFFVWLHYYSVRDTLLGPGRPYRAID VRRNIFDLSAPEKDKFFAYLTLAKHTISSDKKGHGHSYTTAEEAAGIGILTVILGVLLLIFVYVWKTWGQYWQVLGGPVSGLSIGTGRAMGGPVSGLS IGTGRAMLGTHTMEVTVYHRRGISTAPVQMPTAESTGMTPEKVPVSEVMGTTFSSWQIVCSRLEEYNSHQSLCNGTPEGPLRDPIFVVLHSFTDAIFD EWMKRFNPPADAWPHMLARACQHAQGIARLHKRQRPVHQGFGLKLLTVLTVVTGSGHASSTPGGEKETSATQRSFCSCPIGENSPLLSGQQVAATFSF ${\tt RNALEGFDKADGTLDSQVMSLHNLVHSHQSLCNGTPEGPLRRNPGNHDKSRTPRLPPFFPPVTNEELFLTSDQLGYSYAIDLPVSVERKKPPVIRQNI$ HSLSPQEREQFLGALDLAQELAPIGHNRMYNMVPFFPPVTNEELFLTSEVSIVVLSGTTAAQVTTTEWVETTARELPITSPQLSTGVSFFFLSFHISN LQFNSSLEDPYHTHGRYVPPSSTDRSPYEKVSAGNGGSSLLFLSLGLVSLVENALVVATIAKNRNLHSPMSFLNGTNALPHSAANDPIFVVLHSFTDA I_FAVCOCRRKNYGQLDIFPARDTYHPMSEYPTVFFLAMLVLMAVLYVHMLARACQHAQGIARSTNSFRNTVEGYSDPTGKYDPAVRSLHNLALPYWNF ATGKNVCDICTDDLMGSRSNFDSTITDQVPFSVSVSQLRALDGGNKHFLRNQPLFHISNLQFNSSLEDPSTDYYQELQRDISEMSPYEKVSAGNGGSS LSYTNPAVAAASANLAYVIPIGTYGQMKNGSTPMFNDINIYDLFVWRLCQPVLPSPACQLVLHQILKGGSGTYCLNRYGSFSVTLDIVQGIESAEILQ ${\tt AVPSGEGDHAFVDSIFEQWLQRHRPLQEVYPEANAPICTDDLMGSRSNFDSTLISPNSVFSQWRVVCFPARDTYHPMSEYPTYHTHGRYVPPSSTDR$ SYTNPAVAASANLAAEHPTCGCIFKNFNLFLALIICNAIIDPLIYMSQVQGSANDPIFLLHHAFVDSIFEQWLQRRNSMKLPTLKDIRDCLSLQKFD NPPFFONSLISRALVVTHTYLEPGPVTAQVVLQAAIPLSFALPYWNFATGRNECDVCTDQLFGAARPDVIGALLAVGATKVPRNQDWLGVSRQLRTKA ${ t ALDGGNKHFLRNQPLTFALQLHDPSGYLAECDVCTDQLFGAARPDDPTLISRNSRFSSWEAAMPREDAHFIYGYPKKGHGHSYTTAEEAATGKYDPAV$ ${ t RSLHNLAHLFLNGTGGQTHLSSSDVSVSDVPFPFSAQSGAGVPGWGIALLVLSPQEREQFLGALDLAKKRVHPDYVITTQHWFFAYLTLAKHTISSDY$ VIPIGTYGQMKNGSGTNVLETAVILLLEAGALVARAAVLQQLDNVCVLVALAIVYLIALAVCQCRRKNYGQLDICPQEGFDHRDSKVSLQEKNCEPVV PNAPPASVLSSHSPGSGSSTTQGQDVTLAPATEPASDEWMKRFNPPADAWPQELAPIGHNRMYNMVAFHSQELRRTLKEVLTCSWAAFSHQGPAFVTW HRYHLLCLERDLQRLIGNERPMVQRLPEPQDVAQCLEVGLFDTPPFYSNQDPIFVLLHTFTDAVFDEWLRRYNADISTFLGAESANVCGSQQGRGQCTEVRADTRPWSGYNCGDCKFGWTGPNCERKKPPVIRQNIHSLHLFLNGTGGQTHLSSQDPIFVLLHTFTDAVGLVSLLCRHKRKQLPEEKQPLLMEKED YHSGCKILPGAQGQFPRVCMTVDSLVNKECCPRQLPHSSSHWLRLPRIFCSCPIGENSPLLSGDGGPCPSGSWSQKRSFVYVWKTWGQYWQVLNQDWL GVSRQLRTKAWNRQLYPEWTEAQRLIWRDIDFAHEAPAFLPWHRLFLLRWEQEIQAAMTPGTQSPFFLLLLLTVLTVVTGSGHASDKSLHVGTQCALT RRCPOEGFDHRDSKVSLNVTSASGSASGSASTLVHNGTSARATTTPALEGFASPLTG1ADASQSSMHNALH1YMNGTRDTLLGPGRPYRA1DFSHQGP AFVTWHRYHAAMLLAVLYCLLWSFQTSAGHFPRACVSSKAFELTVSCQGGLPKEACMEISSPGCQPPAQVDDRESWPSVFYNRTCQCSGNFMGFNCGN CESAEILQAVPSGEGDAFELTVSCQGGLPKETVCDSLDDYNHLVTLCNGTYEGLLRRNQMGLLSNAPLGPQFPFTGVDDRESWPSVFYNRTYEKLSAE QSPPPYSPAAIVGILLVLMAVVLASLIYRRRLMKQDFSVPGIGILTVILGVLLLIGCWYCRRRNGYRALMYSYLQDSDPDSFQDYIKSYLEQASRIWS WLQGQDVTLAPATEPASGSAATWGQDVTSVPVTSCGSSPVPGTTDGHRPTAEAPNTTAGQVPLVHNGTSARATTTPASKSTPFSIPSHHSDTEETPGW PTTLLVVMGTLVALVGLFVLLAFLTTTEWVETTARELPIPEPEGPDASSIMSTEGAVTLTILLGIFFLCWGPFFLHLTLIVLCPLGAAMVGAVLTALL ${\tt AGLVSLLCRHKRKQLPGALVARAAVLQQLDNVIDVITCSSMLSSLCMTPEKVPVSEVMGTTLAEMSTPEATGMTPAQTSAGHFPRACVSSKNLMEKEC$ CPPWSGDRALRYHSIVTLPRAPRAVAAIWVASVVFSTLFREGTINVHDVETQFNQYKTEAASRYNLTINLMEKECCPPWSGDRSPCGQLSGRGSCQNI IKSYLEQASRIWSWLLGAAMVGAVLTALLAPTTLASHSTKTDASSTHHSSVPPLTSSNHSSGAGVPGWGIALLVLVCVLVALAIVYLIALFLGAIAVD RYISIFYALRYHSIVTLPRAPRLIMPGQEAGLGQVPLIVGILLVLMAVVLASTLVALVGLFVLLAFLQYRRLRKGYTPLMETLISPNSVFSQWRVVCD SLEDYDTLGTLCNSLNSTPTAIPQLGLAANQTGARCLEVSISDGHRPLQEVYPEANAPIGHNRESYMVPFIPLYEPSGTTSVQVPTTEVISTAPVQMP TAESTGKKRVHPDYVITTQHWLGLLGPNGTQPQFANLHQILKGGSGTYCLNVSLADTNSLAVVSTQPEPEGPDASSIMSTESITGSLGPLLDGTATSI TGSLGPLLDGTATLRLVKRQVPLDCVLYDCWRGGQVSLKVSNDGPTLIGANASFSIAL

Synthetic DNA:

 ${\tt TGGAATAGGCAACTGTATCCCGAATGGACAGAGGCTCAGAGACTGGATTGCTGGAGGGGGAGGCCAAGTGTCCCTGAAAGTGTCCAACGATCCCTATAT$ TTATCTCCAGCAAAGACCTCGGCTATGACTATAGCTATCTGCAAGACTCCGACCCTGACTCCTTCCAAGACTATGCCGCTCCCGCTTTCCTCACCTGG CACAGATACCATCTGCTCAGGCTCGAGAAAGACATGCAGGAAATGCTCCAGGAACCCTCCTTCTCCGGCCATAACAGAGAGTCCTACATGGTGCCTTT $\tt CCCTCCGGCACACCTCCGTGCAAGTGCCTACCACAGAGGTCAGCACAGACTATTACCAAGAGCTCCAGAGAGACATTAGCGAAATGTTTCTGCAAAT$ CTATAAGCAAGGCGGATTCCTCGGCCTCAGCAATGCCTGTATGGAAATCTCCAGCCCTGGCTGTCAGCCTCCCGCTCAGAGACTGTGTCAGCCTGTGC GAAACCAATACAAAACCGAAGCCGCTAGCAGATACAATCTGACAATCTCCGACGTCAGCGTCAGCGATGTGCCTTTCCCTTTCTCCGCCCAAGCCGCT ATGTCCCCCCTCTGGTGGGGCTTTCTGCTCAGCTGTCTGGGATGCAAAATCCTCCCCGGAGCCCAAGGCCAATTCCCTAGGGTCGCCGATCTGTCCTA AAGCCACAGGCATGACCCCTGCCGAAGTGTCCATCGTCGTGCTCAGCGGAACCACAGCCGCTCAGGTCATCAAATTCAGACCCGGAAGCGTCGTGGTC CAGCTCACCCTCGCCTTTAGGGAAGGCACAATCAATGTGCATGACGTCGAGACACAGTTTGGCTCCGCCGCTACCTGGGGCCAAGACGTCACCTCCGT GCCTGTGACAAGGCCTGCCCTCGGCTCCACCACCCCCTGCCCATGACGTCCTGCATAAGAGACAGAGACCCGTCCACCAAGGCTTTGGCCTCAAGG

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CACATGCAATGGCACATACGAAGGCCTCCTGAGAAGGAATCAGATGGGCAGAAACTCCATGAAACTGCCTACCCTCAAGGATATCAGAGACTGTACCC TACGATCACGTCGCCGTCCTCGCTCGTCGTCTTCTTCTTCTGCCTATGCTCGTCGTCTCATGCTCTACGTCAAGCTCACCTCAAGCTCACCGAGACGAAAA $\tt CTTTACCATTCCCTATTGGGATTGGAGAGACGCTGAGAAATGCGATATCTGTACCGATGAGTATATGGGACTGAGACTGGTCAAGAGACAGGTCCCCC$ TCGACTGTGTGCTCTACAGATACGGAAGCTTTAGCGTCACCCTCGACATTGTGCAAGGCATTTTCCTCCAGATTTACAAACAGGGAGGCTTTCTGGGA ${\tt CTGTCCAACATTAAGTTTAGGCCTGGCTCCGTGGTCGTGCAACTGACACTGGCTGTGATTGACGTCATCACATGCTCCAGCATGCTGCCAGCCTGTG$ ${ t CTGACGTCGAGTTTTGCCTCAGCCTCACCCAATACGAATTCGATGAGTGGCTGAGAAGGTATAACGCTGACATTAGCACATTCCCTCTGGAAAACGCT$ ${\tt AGGAGAAACGGATACAGAGCCCTCATGGATAAGTCCCTGCATGTGGGAACCCAATGCGCTCTGACAAGGAGACCCTGGCACAGACTGTTTCTGCTCAG$ ${\tt GTGGGAGCAAGAGATTCAGAAACTGACAGGCGATGAGAATTTCACAATCCCTTACTGGGACTGGGCCGCTATGGCTGTGCAAGGCTCCCAGAGAAGGC$ ${\tt TCCTGGGAAGCCTCAACTCCACCCCTACCGCTATCCCTCAGCTCGGCCTCGCCGCTGTGGTCGCCACAATCGCTAAGAATAGGAATCTGCATAGCCCT$ ATGTATTGCTTTATCTGTTGCCTCGCCCTCAGCGATCTGCTCGTTGCTCCAGTCCAGCATATGCCCTCCACATTTACATGAACGGAACCATGAG ${\tt CCAAGTGCAAGGCTCCGCCAATGACCCTATCTTTCTGCTCGGCCAACACCCCTACCAATCCCAATCTGCTCAGCCCTGCCTCCTTCTTTAGCTCCTGGC$ AAATCGTCTGCTCCAGGCTCGAGGAATACAATTACTGTTTCATTTGCTGTCTGGCTCTGTCCGACCTCCTGGTCAGCGGAACCAATGTGCTCGAGACAGCCGTCATCCTCCTGCTCGAGGCTGACCCTACCCTCATCTCCAGGAATAGCAGATTCTCCAGCTGGGAGACAGTGTGTGACTCCCTGGATGACTATAA CCATCTGGTCACCCTCACCAGACCCGCTCTGGGAAGCACAACCCCTCCCGCTCACGATGTGACAAGCCCTCCCGATAACAAAGCCGCTAGGGATGCCG AAAAGTGTGACATTTGCACAGACGAATACATGGGCGGACAGCATCCCACAAACCCTAACCTCCTGTCCCCGCTAGCTTTACCTTTGCCCTCCAGCTC CACGATCCCTCCGGCTATCTGGCTGAGGCTGACCTCAGCTATACCTGGGACTTTGGCGATAGCTCCGGCACAAGCTCCGCCGATGTGGAATTCTGTCT $\tt GTCCCTGACACAGTATGAGTCCGGCTCCATGGATAAGGCTGCCAATTTCTCCTTCAGAAACACAGGCCCTACCCTCATCGGAGCCAATGCCTCCTTCT$ $\tt CCATCGCTCTGAATTTCCCTGGCTCCCAGAAAGTGCTCCCCGATGGCCAAGTGATTTGGGGACCCTTTTTCCTCCACCTCACCCTCATCGTCCTGTGT$ $\tt CCCGAACACCCTACCTGTGGCTGTATCTTTAAGAATTTCAATCTGTTTTGCCAATGCTCCGGCAATTTCATGGGCTTTAACTGTGGCAATTGCAAATT$ CGGATTCTGGGGCCCTAACTGTACCGAAAGGAGACTGCTCCAGTATAGGAGACTGAGAAAGGGATACACCCCTCATGGAAACCCATCTGTCCAGCA AAAGGTATACCGAAGAGGCTGCCGCTCCCCTCGAGAATGCCCCTATCGGACACAATAGGCCATACAATATGGTCCCCTTTTGGCCTCCCGTCACCAAT GTGGGGCGGAAGGCCTACCGCTGAGGCTCCCAATACCACAGCCGGACAGGTCCCCACAACCGAAGTGGTCGGCACAACCCCTGGCCAAGCCCCTACCG CTAGCACACCCGGAGGCGAAAAGGAAACCTCCGCCACAGAGAGAAGCTCCGTGCCTAGCTCCAACAAAAGAATGCCGTCAGCATGACCTCGCTGATT TACAGAAGGAGACTGATGAAGCAAGACTTTAGCGTCCCCAACTGCCTCACTCCAGCTCCCACTGGCTGAGACTGCCTAGGATTCTGGGACTGCTCGG ${\tt CCCTAACGGAACCCCAATTCGCTAACTGTAGCGTCTACGATTTCTTTGTGTGGCTGCATTACTATAGCGTCTGCCTCGAGGTCGGCCTCTTCG$ ATACCCCTCCTTTTACTCCAACTCCACCAATAGCTTTAGGAATACCGTCGAGGGATACTCCGACCCTGCCGCTATGGATCTGGTCCTGAAAAGGTGT CTGCTCCACCTCGCCGTCATCGGAGCCCTCCTGGCTGTGGGAGCCACAAAGGTCCCCAGAAACCAAACCGGAGCCAGATGCCTCGAGGTCAGCATTAG ${\tt TCGAGGGATTCGCTAGCCCTCTGACAGGCATTGCCGATGCCTCCAGCCCTTGCGGACAGCTCAGCGGAAGGCGGAAGCTCTCAGAATATCCTCCTGTCC$ AACGCTCCCCTCGGCCCTCAGTTTCCCTTTACCGGAATGCATTACTATGTGTCCATGGATGCCCTCCTGGGAGGCTCCGAGATTTGGAGACACTTGA CTTTGCCCATGAGGCTCCCGCTTTCCTCGAGGAAAAGCAACCCCTCCTGATGGAGAAAGAGGATTACCATAGCCTCTACCAAAGCCATCTGGCTGCCG GCCAATGCACAGAGGTCAGGGCTGACACAAGGCCTTGGTCCGGCCCTTACATTCTGAGAAACCAAGACGATAGGGAACTGTGGCCCAGAAGCGTCCCC ${ t TCCAGCACAGAGAAAAACGCTGTGTCCATGACAAGCTCCGTGCTCAGCTCCCCACTCCCCGGAAGCGGAAGCTCCACCACAACCCCTATGTTTAACGA$ $\tt CTCTGCAATAGCACAGAGGATGGCCCTATCAGAAGGAATCCCGCTGGCAATGTGGCTTGGGTCAACAATACCATTATCAATGGCTCCCAGGTCTGGGG$ ${f AGAAACTGTCCGCCGAACAGTCCCCCCCCCCCTATAGCCCTAGCAGAAGCTATGTGCCTCTGGCTCAGCTCCAGCTCCGCCTTTACCATTACCGATCAG$ GTCCCCTTTAGCGTCAGCGTCAGCCAACTGGAGACTGGAAAAGGATATGCAAGAGATGCTGCAAGAGCCTAGCTTTAGCCTCCCCTATTGGAATTTCGC TACCGGAAAGAATGTGTGTGACATTGTGCCTTTCTGGCCCCCTGTGACAACACAGAGATGTTCGTCACCGCTCCCGATAACCTCGGCTATACCTATG AGGCTGCCTGCTCGTGTATGACTTTTTCGTCTGGCTCCACTATTACTCCGTGAGAGACACACTGCTCGGCCCCTGGCAGACCCTATAGGGCTATCGAT GTGAGAAGGAATATCTTTGACCTCAGCGCTCCCGAAAAGGATAAGTTTTTCGCTTACCTCACCCTCGCCAAACACACAATCTCCAGCGATAAGAAAGG AAACCTGGGGCCAATACTGGCAGGTCCTGGGAGGCCCTGTGTCCGGCCTCAGCATTGGCACAGGCCAGAGCCATGGGCGGACCCGTCAGCGGACTGTCC $\tt CGAAAGCACAGGCATGACCCCTGAGAAAGTGCCTGTGTCCGAGGTCATGGGAACCACATTCTCCAGCTGGCAGATTGTGTGTAGCAGACTGGAAGAGT$ A TAACTCCCACCAAAGCCTCTGCAATGGCACCCCGAAGGCCCTCTGAGAGACCCTATCTTTGTGGTCCTGCATAGCTTTACCGATGCCATTTTCGATGCAAAGGCCTGTGCATCAGGGATTCGGACTGAAACTGCTCACCGTCCTGACAGTGGTCACCGGAAGCGGACACGCTAGCTCCACCCCTGGCGGAGAGA ${\tt AAGAGACAAGCGCTACCCAAAGGTCCTTCTGTAGCTGTCCCATTGGCGAAAACTCCCCCCTCCTGTCCGGCCAACAGGTCGCCGCTACCTTTAGCTTT}$ AGGAATGCCCTCGAGGGATTCGATAAGGCTGACGGAACCCTCGACTCCCAGGTCATGTCCCTGCATAACCTCGTGCATAGCCATCAGTCCCTGTGTAA $\tt GCCTTTCTTTCCCCCTGTGACAAACGAAGAGCTCTTCCTCACCTCCGAGGTCAGCATTGTGGTCCTGTCCGGCACAACCGCTGCCCAAGTGACAACCA$ ${\tt CAGAGTGGGTGGAAACCACAGCCAGAGAGCTCCCCCATTACCTCCCCCCAACTGTCCACCGGAGTGTCCTTCTTTTTCCTCAGGCTTTCACATTAGCAATTAGAATTAGCAATTAGCAATTAGCAATTAGAATT$ $\tt CTGCAATTCAATAGCTCCCTGGAAGACCCTTACCATACCCATGGCAGGATACGTCCCCCTAGCTCCACCGATAGGTCCCCCTATGAGAAAGTGTCCGC$ CGGAAACGGAGGCTCCAGCCTCCTGTTTCTGTCCCTGGGACTGGTCAGCCTCGTGGAAAACGCTCTGGTCGTGGCTACCATTGCCAAAAACAGAAACC ATCTTTGCCGTCTGCCAATGCAGAAGGAAAACTATGGCCAACTGGATATCTTTCCCGCTAGGGATACCTATCACCCTATGTCCGAGTATCCCACAGT GTTTTTCCTCGCCATGCTGGTCCTGATGGCCGTCCTGTATGTGCATATGCTCGCCAGAGCCTGTCAGCATGCCCAAAGCCATTGCCAGAAGCACAAACT

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 $\tt CCTTCAGAAACACAGTGGAAGGCTATAGCGATCCCACAGGCAAATACGATCCCGCTGTGAGAAGCCTCCACAATCTGGCTCTGCCTTACTGGAACTTT$ $\tt GTCCGTGTCCCAGCTCAGGGCTCTGGATGGCGGAAACAACACTTTCTGAGAAACCACTCTTCCATATCTCCAACCTCCAGCTTTAACTCCAGCC$ CATGTTCAATGACATTAACATTTACGATCTGTTTGTGTGGAGGCTCTGCCAACCCGTCCTGCCTAGCCCTGTCCTGTCAGCTCCTACCAAATCC GCCGTCCCTCCGGCGAAGGCGATCACCATGCCTTTGTGGATAGCATTTTCGAACAGTGGCTGCAAAGGCATAGGCCTCTGCAAGAGGTCTACCCTGA GGCTAACGCTCCCATTTGCACAGACGATCTGATGGGCTCCAGGTCCAACTTTGACTCCACCCTCATCTCCCCCAATAGCGTCTTCTCCCAGTGGAGGG ${\tt AGCTATACCAATCCCGCTGTGGCTGCCGCTAGCGCTAACCTCGCCGCTGAGCATCCCACATGCGGATGCATTTTCAAAAACTTTAACCTCTTCCTCGC$ TCGACTCCATCTTGAGCAATGGCTCCAGAGAAGGAATAGCATGAAGCTCCCACACTGAAAGACATTAGGGATTGCCTCAGCCTCCAGAAATTCGAT AACCCTCCCTTTTTCCAAAACTCCCTGATTAGCAGAGCCCTCGTGGTCACCCATACCTATCTGGAACCCGGACCCGTCACCGCTCAGGTCCTCCCA GACCCGATGTGATTGGCGCTCTGCTCGCCGTCGGCGTACCAAAGTGCCTAGGAATCAGGATTGGCTCGGCGTCAGCACACACCTCAGGACAAAGGCT GCCCTCGACGGAGGCAATAAGCATTTCCTCAGGAATCAGCCTCTGACATTCGCTCTGCAACTGCATGACCCTAGCGGATACCTCGCCGAATGCGATGT $\tt GTGTACCGATCAGCTCTTCGGAGCCGCTAGGCCTGACGATCCCACACTGATTAGCAGAAACTCCAGGTTTAGCTCCTGGGAAGCCGCTATGCCTAGGG$ GTGATTCCCATTGGCACATACGGACAGATGAAGAATGGCTCCGGCACAAACGTCCTGGAAACCGCTGTGATTCTGCTCCTGGAAGCCGGAGCCCTCGT GAAAGAATTACGGACAGCTCGACATTTGCCCTCAGGAAGGCTTTGACCATAGGGATAGCAAAGTGTCCCTGCAAGAGAAAAACTGTGAGCCTGTGGTC GCCTGCCTCCGACGAATGGATGAAGAGATTCAATCCCCCTGCCGATGCCTGGCCCCAAGAGCTCGCCCCTATCGGACACAATAGGATGTACAATATGG ${ t TCGCCTTTCACTCCCAGGAACTGAGAAGGACACTGAAAGAGGTCCTGACATGCTCCTGGGCTGCCTTCTCCCACCAAGGCCCTGCCTTTGTGACATGG$ tcagtgtctggaagtgggactgtttgacacaccctttctatagcaatcaggatcccattttcgtcctgctccacacattcacagacgctgtgttg GAAGTGAGAGCCGATACCAGACCCTGGAGCGGATACAATTGCGGAGACTGTAAGTTTGGCTGGACCGGACCCAATTGCGAAAGGAAAAAGCCTCCCGT CCTTTACCGATGCCGTCGGCCTCGTGTCCCTGCTCTGCAGACACAAAAGGAAACAGCTCCCCGAAGAAAACAGCCTCTGCTCATGGAAAAAGGAAGAC GCCCTTGCCCTAGCGGAAGCTGGAGCCAAAAGAGCTTTGTGTATGTGTGGAAGACATGGGGAACAGTATTGGCAAGTGCTCAACCAAGACTGGCTG ${\tt TCACGAAGCCCTGCCTTTCTGCCTTGGCATAGGCTCTTCCTCCTGAGATGGGAACAGGGAAATCCAAGCCGCTATGACACCCGGAACCCAAAGCCCTT}$ AGAAGGTGTCCCCAAGAGGGATTCGATCACAGAGACTCCAAGGTCAGCCTCAACGTCACCTCCGGCTCCGGCTCCGGCTCCGGCTCCGCCTCCACCCT CGTGCATAACGGAACCTCCGCCAGAGCCACAACCACACCCGCTCTGGAAGGCTTTGCCTCCCCCCTCACCGGAATCGCTGACGCTAGCCAAAGCTCCA TGCATAACGCTCTGCATATCTATATGAATGGCACAAGGGATACCCTCCTGGGACCCGGAAGGCCTTACAGAGCCATTGACTTTAGCCATCAGGGACCC ${ t GCTTTCGTCACCTGGCACAGATACCATGCCGCTATGCTCCTGGCTGTGCTCTACTGTCTGGTCCTTCCAAACCTCCGCCGGACACTTTCCCAG$ AGCCTGTGTGTCCAGCAAAGCCTTTGAGCTCACCGTCAGCTGTCAGGGGAGGCCTCCCCAAAGAGGGCTTGCATGGAGATTAGCTCCCCCGGATGCCAAC $\tt TGTGAGTCCGCCGAAATCCTCCAGGCTGTGCCTAGCGGAGAGGGAGACGCTTTCGAACTGACAGTGTCCTGCCAAGGCGGACTGCCTAAGGAAACCGT$ $\tt CTGCGATAGCCTCGACGATTACAATCACCTCGTGACACTGTGTAACGGAACCTATGAGGGACTGCTCAGGAGAAACCAAATGGGACTGCTCAGCAATG$ CCCTCTGGGACCCCAATTCCCTTTCACAGGCGTCGACGATAGGGAAAGCTGGCCCTCCGTGTTTTACAATAGGACATACGAAAAGCTCAGCGCTGAG CAAAGCCCTCCCCTTACTCCCCCGCTGCCATCGTCGGCATTCTGCTCGTGCTCATGGCTGTGCTCTGGCTAGCCTCATCTATAGGAGAAGGCTCAT GAAACAGGATTTCTCCGTGCCTGGCATTGGCATTCTGACAGTGATTCTGGGAGTGCTCCTGCTCATCGGATGCTGGTACTGTAGGAGAAGGAATGGCT ATAGGGCTCTGATGTACTCCTACCTCCAGGATAGCGATCCCGATAGCTTTCAGGATTACATTAAGTCCTACCTCGAGCAAGCCTCCAGGATTTGGTCC TGGCTCCAGGGACAGGATGTGACACTGGCTCCCGCTACCGAACCCGCTAGCGGAAGCGTGCCACATGGGGACAGGATGTGACAAGCGTCCCCGTCAC $\tt CGCTAGGGAACTGCCTATCCCTGAGGCACCCGATGCCTCCAGCATTATGTCCACCGAAGGCGCTGTGACACTGACAATCCTCCTGGGAATCT$ ${\tt GCCGGACTGGTCAGCCTCTGTGTAGGCATAAGAGAAAGCAACTGCCTGGCGCTCTGGTCGCCAGAGCCGCTGTGCTCCAGCAACTGGATAACGTCAT}$ CGATGTGATTACCTGTAGCTCCATGCTCAGCTCCCTGTGTATGACACCCGAAAAGGTCCCCGTCAGCGAAGTGATGGGCACAACCCTCGCCGAAATGT CCTCGCCTCCCACTCCACCAAAACCGATGCCTCCAGCACACCCCTAGCTGCCTCCCCTCACCTCCAGCAATCACTCCAGCGGAGCCGGAGTGC ${\tt AGGTATATCTCCATCTTTTACGCTCTGAGATACCATAGCATTGTGACACTGCCTAGGGCTCCCAGACTGATTATGCCTGGCCAAGAGGCTGGCCTCGGCCTGGCCTGGCCTGGCCTCGGCCTGGCTGGCTGGCTGGCTGGCTGGCCTGGCTGGCTGGCTGGCCTGGCCTGGCTGGCTGGCTGGCTGGCTGGCTGGCTGGCTGGCCTGGCCTGGCCTGGCCTGGCCTGGCCTGGCCTGGCCTGGCCTGGCCTGGCTGGCCTGGCCTGGCCTGGCCT$ ${\tt TTCTGCAATACAGAAGGCTCAGGAAAGGCTATACCCCTCTGATGGAGACACTGATTAGCCCTAACTCCGTGTTTAGCCCAATGGAGAGTGGTCTGCGATTGCAATTGCA$ AGCCTCGAGGATTACGATACCCTCGGCACACTGTGTAACTCCCTGAATAGCACACCCACAGCCATTCCCCAACTGGGACTGGCTGCCAATCAGACAGG $\tt CGCTAGGTGTCTGGAAGTGTCCATCTCCGACGGACACAGACCCCTCCAGGAAGTGTATCCCGAAGCCAATGCCCCTATCGGACACAATAGGGAAAGCT$

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Melanoma cancer Specific Savine Scramble process
 Scramble - Output File
 Scramble version: 0.1 beta, 08/02/1999
Num. genes : 10
Num. segments : 121
 Segment length
             : 30
Segment overlap : 15
Segments in original order:
Gene
        : BAGE
Segment# : 1
Offset
       : 1
1st Codon : 1
 A A M A A R A V F L A L S A Q L L Q A R L M K E E S P V V S
Segment# : 2
       : 16
1st Codon : 1
 LLQARLMKEESPVVSWRLEPEDGTALCFIF
\tt CTGCTCCAGGCTAGGCTCATGAAAGAGGAAAGCCCTGTGGTCAGCTGGAGGCTCGAGCCTGAGGATGGCACAGCCCTCTGCTTTATCTTT
Gene
        : BAGE
Segment# : 3
Offset
       : 31
1st Codon : 1
 WRLEPEDGTALCFIFAA
TGGAGACTGGAACCCGAAGACGGAACCGCTCTGTGTTTCATTTTCGCTGCC
       : GAGE-1
Gene
Segment# : 1
Offset
       : 1
1st Codon : 1
A A M S W R G R S T Y R P R P R R Y V E P P E M I G P M R P
{\tt GCCGCTATGTCCTGGAGAGGCAGAAGCACATACAGACCCAGAACCCAGAAGGTATGTGGAACCCCCTGAGATGATCGGACCCATGAGGCCT}
       : GAGE-1
Segment# : 2
Offset
       : 16
1st Codon : 1
RRYVEPPEMIGPMRPEQFSDEVEPATPEEG
AGGAGATACGTCGAGCCTCCCGAAATGATTGGCCCTATGAGACCCGAACAGTTTAGCGATGAGGTCGAGCCTGCCACACCCGAAGAGGGA
       : GAGE-1
Gene
Segment# : 3
Offset
       : 31
1st Codon : 1
E Q F S D E V E P A T P E E G E P A T Q R Q D P A A A Q E G
GAGCAATTCTCCGACGAAGTGGAACCCGCTACCCCTGAGGAAGGCGAACCCGCTACCCAAGAGGCAAGACCCTGCCCCAAGAGGGA
       : GAGE-1
Segment# : 4
Offset
       : 46
E P A T Q R Q D P A A A Q E G E D E G A S A G Q G P K P E A
Gene
       : GAGE-1
Segment# : 5
Offset
       : 61
1st Codon : 1
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Figure 27 (Cont)

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E D E G A S A G Q G P K P E A D S Q E Q G H P Q T G C E C E $\tt GAGGATGAGGGAGCCTCCGCCGGACAGGGACCCAAACCCGAAGCCGATAGCCAAGGCCATCCCCAAACCGGATGCGAAGCCAAGCCGAAGCCAAGCCGGAAGCCCGAAGCCCGAAGCCCGAAGCCCGAAGCCCGAAGCCCGAAGCCCGAAGCCCGAAGCCCGAAGCCCAAGCCCGAAGCCCGAAGCCCGAAGCCCGAAGCCCGAAGCCCGAAGCCCGAAGCCCGAAGCCCGAAGCCCGAAGCCCGAAGCCCGAAGCCCGAAGCCCAAGCCCGAAGCCCAAGCCCGAAGCCCAAGCCCGAAGCCCAAGCCCGAAGCCCAAGCCCCAAGCCCGAAGCCCAAGCCCAAGCCCAAGCCCAAGCCCAAGCCCAAGCCCCAAGCCCCAAGCCCAAGCCCAAGCCCCAAGCCCAAGCCCAAGCCCAAGCCCAAGCCCCAAGCCCCAAGCCCAAGCCCAAGCCCAAGCCCAAGCCCAAGCCCAAGCCCAAGCCCAAGCCCAAGCCCAAGCCCAAGCCCAAGCCCAAGCCCCAAGCCCCAAGCCCCAAGCCCAAGCCCAAGCCCAAGCCCAAGCCCCAAGCCCAAGCCCAAGCCCAAGCCCCAAGCCCAAGCCCAAGCCCAAGCCCAAGCCCAAGCCCAAGCCCAAGCCCAAGCCCAAGCCCAAGCCCAAGCCCAAGCCCCAAGCCCAAGCCCAAGCCCAAGCCCAAGCCCAAGCCCAAGCCCAAGCCCAAGCCAAGCCAAGCCAAGCCAAGCCCAAGCCAAGCCAAGCCAAGCCAAGCCAAGCCAAGCCAAGCCAAGCCAAGCCAAGCCAAGCAAGCAAGCAAGCAAGCAAGCAAGCAAGCAAGCAAGCAAGCAAGCAAGCAAGCAAGCAAGCAAGCAAAGCCAAGCAAGCAAGCAAGCAAGCAAGCAAGCAAGCAAGCAAGCAAGCAAGCAAGCAAGCAAGCAAAGCAAAGCAAGCAAAGCAAAGCAAAGCAAGCAAAGCAAAGCAAAGCAAAGCAAAGCAAAGCAAAGCAAAGCAAAGCAAAGCAAAGCAAAGCAAAGCAAAGCAAAGCAAAGCAAAGCCCAAGCAAGCAAGCCAAGCAAGCAAGCCAAGCCAAGCACAAGCACAAGCACAAGCAA$: GAGE-1 Segment# : 6 Offset : 76 1st Codon : 1 D S Q E Q G H P Q T G C E C E D G P D G Q E M D P P N P E E GACTCCCAGGAACAGGGACACCCTCAGACAGGCTGTGAGTGTGAGGATGGCCCTGACGGACAGGAAATGGATCCCCCTAACCCTGAGGAA Gene : GAGE-1 Segment# : 7 Offset : 91 1st Codon : 1 D G P D G Q E M D P P N P E E V K T P E E E M R S H Y V A Q GACGGACCCGATGGCCAAGAGATGGACCCTCCCAATCCCGAAGAGGTCAAGACACCCGAAGAGAGGAAATGAGAAGCCATTACGTCGCCCAA Gene : GAGE-1 Segment# : 8 : 106 Offset. 1st Codon : 1 V K T P E E E M R S H Y V A Q T G I L W L L M N N C F L N L $\tt GTGAAAACCCCTGAGGAAGAGATGAGGTCCCACTATGTGGCTCAGACAGGCATTCTGTGGCTGCTCATGAATAACTGTTTCCTCAACCTC$: GAGE-1 Gene Segment# : 9 Offset : 121 1st Codon : 1 T G I L W L L M N N C F L N L S P R K P A A ACCGGAATCCTCTGGCTCCTGATGAACAATTGCTTTCTGAATCTGTCCCCCAGAAAGCCTGCCGCT : gp100In4 Segment# : 1 Offset : 1 1st Codon : 1 A A S W S Q K R S F V Y · V W K T W G E G L P S Q P I I H T C ${\tt GCCGCTAGCTGGAGCCAAAAGAGAAGCTTTGTGTATGTGTGGAAGACATGGGGAGAGGGACTGCCTAGCCAACCCATTATCCATACCTGT}$ Gene : gp100In4 Segment# : 2 Offset : 16 1st Codon : 1 T W G E G L P S Q P I I H T C V Y F F L P D H L S F G R P F ${\tt ACCTGGGGCGAAGGCCTCCCCAGCCTATCATTCACACATGCGTCTACTTTTTCCTCCCCGATCACCTCAGCTTTGGCAGACCCTTT$ Gene : gp100In4 Segment# : 3 Offset. : 31 V Y F F L P D H L S F G R P F H L N F C D F L A A $\tt GTGTATTTCTTGCCTGACCATCTGTCCTTCGGAAGGCCTTTCCATCTGAATTTCTGTGACTTTCTGGCTGCC$ Gene : MAGE-1 Segment# : 1 Offset : 1 1st Codon : 1 A A M S L E Q R S L H C K P E E A L E A Q Q E A L G L V C V Gene : MAGE-1 Segment# : 2 Offset 1st Codon : 1 $\begin{smallmatrix} E & A & L & E & A & Q & Q & E & A & L & G & L & V & C & V & Q & A & A & T & S & S & S & P & L & V & L & G & T & L \\ \end{smallmatrix}$ Gene : MAGE-1 Segment# : 3 Offset : 31 1st Codon : 1 Q A A T S S S P L V L G T L E E V P T A G S T D P P Q S P CAGGCTGCCACAAGCTCCAGCTCCCCCCTCGTGCTCGGCACACTGGAAGAGGTCCCCACAGCCCGGAAGCACAGACCCTCCCCAAAGCCCT

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Gene : MAGE-1 Segment# : 4 Offset : 46 1st Codon: 1
E E V P T A G S T D P P Q S P Q G A S A F P T T I N F T R Q Gene : MAGE-1 Segment# : 5 Offset : 61 1st Codon : 1 O G A S A F P T T I N F T R O R O P S E G S S R E E E G P : MAGE-1 Gene Segment# : 6 Offset : 76 1st Codon : 1 R Q P S E G S S S R E E E G P S T S C I L E S L F R A V I T AGGCAACCCTCCGAGGGAAGCTCCAGCAGAGAGGAAGAGGAACCCTCCACCTCCTCCATCTTCTGGAAAGCCTCTTCAGAGCCGTCATCACA Gene : MAGE-1 Segment# : 7 Offset : 91 1st Codon: 1
S T S C I L E S L F R A V I T K K V A D L V G F L L L K Y R : MAGE-1 Gene Segment# : 8 Offset : 106 1st Codon : 1 K K V A D L V G F L L L K Y R A R E P V T K A E M L E S V I AAGAAAGTGGCTGACCTCGTGGGATTCCTCCTGCTCAAGTATAGGGCTAGGGAACCCGTCACCAAAGCCGAAATGCTCGAGTCCGTGATT : MAGE-1 Gene Segment# : 9 Offset : 121 1st Codon : 1 A R E P V T K A E M L E S V I K N Y K H C F P E I F G K A S ${\tt GCCAGAGAGCCTGTGACAAAGGCTGAGATGCTGGAAAGCGTCATCAAAAACTATAAGCATTGCTTTCCCGAAATCTTTGGCAAAGCCTCC}$ Gene : MAGE-1 Segment# : 10 Offset : 136 1st Codon : 1 K N Y K H C F P E I F G K A S E S L Q L V · F G I D V K E A D : MAGE-1 Gene Segment# : 11 Offset : 151 1st Codon : 1 ESLQLVFGIDVKEADPTGHSYVLVTCLGLS GAGTCCCTGCAACTGGTCTTCGGAATCGATGTGAAAGAGGCTGACCCTACCGGACACTCCTACGTCCTGGTCACCTGTCTGGGACTGTCC Gene : MAGE-1 Segment# : 12 Offset : 166 PTGHSYVLVTCLGLSYDGLLGDNOIMPKTG $\tt CCCACAGGCCATAGCTATGTGCTCGTGACATGCCTCGGCCTCAGCTATGACGGACTGCTCGGCGATAACCAAATCATGCCCAAAACCGGA$ Gene : MAGE-1 Segment# : 13 Offset : 181 1st Codon : 1 Y D G L L G D N Q I M P K T G F L I I V L V M I A M E G G H Gene : MAGE-1

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Segment# : 14 : 196 Offset 1st Codon : 1 F L I I V L V M I A M E G G H A P E E E I W E E L S V M E V TTCCTCATCATTGTGCTCGTGATGATCGCTATGGAAGCCGGACACGCTCCCGAAGAGAAATCTGGGAGGAACTGTCCGTGATGGAGGTC : MAGE-1 Segment# : 15 Offset : 211 1st Codon : 1 A P E E E I W E E L S V M E V Y D G R E H S A Y G E P R K L GCCCCTGAGGAAGAGTTTGGGAAGAGCTCAGCGTCATGGAAGTGTATGACGGAAGGGAACACTCCGCCTATGGCGAACCCAGAAAGCTC Gene : MAGE-1. . Segment# : 16 : 226 Offset 1st Codon : 1 Y D G R E H S A Y G E P R K L L T Q D L V Q E K Y L E Y R Q TACGATGGCAGAGAGCATAGCGCTTACGGAGAGCCTAGGAAAACTGCTCACCCAAGACCTCGTGCAAGAGAAATACCTCGAGTATAGGCAA Gene : MAGE-1 Segment# : 17 Offset : 241 1st Codon : 1 L T Q D L V Q E K Y L E Y R Q V P D S D P A R Y E F L W G P : MAGE-1 Gene : 18 Segment# Offset : 256 1st Codon: 1 VPDSDPARYEFLWGPRALAETSYVKVLEYV ${\tt GTGCCTGACTCCGACCCTGCCAGATACGAATTCCTCTGGGGACCCAGAGCCCTCGCCGAAACCTCCTACGTCAAGGTCCTGGAATACGTC}$: MAGE-1 Gene Segment# : 19 Offset : 271 1st Codon : 1 RALAETSYVKVLEYVIKVSARVRFFFPSLR : MAGE-1 Gene Segment# : 20 Offset : 286 1st Codon : 1 I K V S A R V R F F F P S L R E A A L R E E E G V A A : MAGE-3 Gene Segment# : 1 : 1 Offset A A M P L E Q R S Q H C K P E E G L E A R G E A L G L V G A GCCGCTATGCCTCTGGAACAGGAGAAGCCAACACTGTAAGCCTGAGGAAGGCCTCGAGGAGGGGAGAGGCTCTGGGACTGGTCGCGCT : MAGE-3 Segment# : 2 Offset : 16 1st Codon : 1 EGLEARGEALGLVGAQAPATEEOEAASS GAGGGACTGGAAGCCAGAGGCGAAGCCCTCGGCCTCGTGGGAGCCCCAAGCCCCTGCCACAGAGGAACAGGAAGCCGCTAGCTCCAGCTCC : MAGE-3 Gene Segment# : 3 : 31 Offset 1st Codon : 1 Q A P A T E E Q E A A S S S S T L V E V T L G E V P A A E S Gene : MAGE-3

Figure 27 (Cont)

Segment# : 4

Offset

: 46

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1st Codon : 1 T L V E V T L G E V P A A E S P D P P Q S P Q G A S S L P T Gene : MAGE-3 Segment# : 5 Offset : 61 1st Codon : 1 P D P P Q S P Q G A S S L P T T M N Y P L W S Q S Y E D S S Segment# : 6 : 76 Offset 1st Codon : 1 T M N Y P L W S Q S Y E D S S N Q E E E G P S T F P D L E S ACCATGAACTATCCCCTCTGGTCCCAGTCCTACGAAGACTCCAGCAATCAGGAAGAAGGCCCTAGCACATTCCCTGACCTCGAGTCC : MAGE-3 Segment# : 7 Offset : 91 1st Codon: 1 NQEEEGPSTFPDLESEFQAALSRKVAELVH AACCAAGAGAGAAGAGGACCCTCCACCTTTCCCGATCTGGAAAGCGAATTCCAAGCCGCTCTGTCCAGGAAAGTGGCTGAGCTCGTGCAT Gene : MAGE-3 Segment# : 8 Offset : 106 1st Codon : 1 E F Q A A L S R K V A E L V H F L L L K Y R A R E P V T K A GAGTTTCAGGCTGCCCTCAGCAGAAAGGTCGCCGAACTGGTCCACTTTCTGCTCCTGAAAATACAGAGCCAGAGAGCCTGTGACAAAGGCT : MAGE-3 Gene Segment# : 9 Offset : 121 1st Codon : 1 F L L L K Y R A R E P V T K A E M L G S V V G N W Q Y F F P ${\tt TTCCTCCTGCTCAAGTATAGGGCTAGGGAACCCGTCACCAAAGCCGAAATGCTCGGCTCCGTGGTCGGCAATTGGCAATACTTTTTCCCT}$: MAGE-3 Segment# : 10 Offset : 136 1st Codon : 1 EMLGSVVGNWQYFFPVIFSKASSSLOLVFG Gene : MAGE-3 Segment# : 11 1st Codon : 1 V I F S K A S S S L Q L V F G I E L M E V D P I G H L Y I F ${\tt GTGATTTCTCCAAGGCTAGCTCCAGCCTCGTGTTTGGCATTGAGCTCATGGAAGTGGATCCCATTGGCCATCTGTATATCTTT}$: MAGE-3 Gene Segment# : 12 Offset : 166 I E L M E V D P I G H L Y I F A T C L G L S Y D G L L G D N ATCGAACTGATGGAGGTCGACCCTATCGGACACCTCTACATTTTCGCTACCTGTCTGGGACTGTCCTACGATGGCCTCCTGGGAGACAAT : MAGE-3 Segment# : 13 Offset : 181 1st Codon : 1 ATCLGLSYDGLLGDNQIMPKAGLLIIVLA GCCACATGCCTCGGCCTCAGCTATGACGGACTGCTCGGCGATAACCAAATCATGCCCCAAAGCCGGACTGCTCATCATTGTGCTCGCCATT : MAGE-3 Gene Segment# : 14 Offset : 196 1st Codon: 1 Q I M P K A G L L I V L A I I A R E G D C A P E E K I W E

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Gene : MAGE-3 Segment# : 15 Offset : 211 1st Codon : 1 I A R E G D C A P E E K I W E E L S V L E V F E G R E D S I : MAGE-3 Gene Segment# : 16 Offset : 226 1st Codon : 1 E L S V L E V F E G R E D S I L G D P K K L L T Q H F V Q E GAGCTCAGCGTCCTGGAAGTGTTTGAGGGAAGGGAAGACTCCATCCTCGGCGATCCCAAAAAGCTCCTGACACAGCATTTCGTCCAGGAA : MAGE-3 Gene } Segment# : 17 Offset : 241 LGDPKKLLTQHFVQENYLEYRQVPGSDPAC $\tt CTGGGAGACCCTAAGAAACTGCTCACCCAACACTTTGTGCAAGAGAATTACCTCGAGTATAGGCAAGTGCCTGGCTCCGACCCTGCTTGT$: MAGE-3 Segment# : 18 Offset : 256 1st Codon : 1 $\begin{smallmatrix} N&Y&L&E&Y&R&Q&V&P&G&S&D&P&A&C&Y&E&F&L&W&G&P&R&A&L&V&E&T&S&Y\end{smallmatrix}$ AACTATCTGGAATACAGACAGGTCCCCGGAAGCGATCCCGCTTGCTATGAGTTTCTGTGGGGCCCTAGGGCTCTGGTCGAGACAAGCTAT Gene : MAGE-3 Segment# : 19 Offset : 271 1st Codon : 1 Y E F L W G P R A L V E T S Y V K V L H H M V K I S G G P H ${\tt TACGAATTCCTCTGGGGAACCCTGGTGGAAACCTCCTACGTCAAGGTCCTGCATCACATGGTGAAAATCTCCGGCGGACCCCAT}$: MAGE-3 Segment# : 20 Offset : 286 1st Codon : 1 V K V L H H M V K I S G G P H I S Y P P L H E W V L R E G E GTGAAAGTGCTCCACCATATGGTCAAGATTAGCGGAGGCCCTCACATTAGCTATCCCCCTCTGCATGAGTGGGTGCTCAGGGAAGGCGAA Gene : MAGE-3 Segment# : 21 Offset : 301 1st Codon : 1 I S Y P P L H E W V L R E G E E A A Gene Segment# : 1 Offset : 1 1st Codon: 1 A A M E R R R L W G S I Q S R Y I S M S V W T S P R R L V E GCCGCTATGGAAAGGAGAAGGCTCTGGGGAAGCATTCAGTCCAGGTATATCTCCATGTCCGTGTGGACCTCCCCAGAAGGCTCGTGGAA Gene : PRAME : 2 Segment# lst Codon: 1
Y I S M S V W T S P R R L V E L A G Q S L L K D E A L A I ${\tt TACATTAGCATGAGCGTCTGGACAAGCCCTAGGAGAGACTGGTCGAGGCTCGCCGGACAGTCCCTGCTCAAGGATGAGGCTCTGGCTATCGCT}$ Gene : PRAME Segment# : 3 Offset : 31 LAGQSLLKDEALAIAALELLPRELFPPLFM

Figure 27 (Cont)

189/216 Gene : PRAME Segment# : 4 Offset : 46 1st Codon : 1 A L E L L P R E L F P P L F M A A F D G R H S Q T L K A M V ${\tt GCCCTCGAGCTCCTGCCTAGGGAACTGTTTCCCCCTCTGTTTATGGCTGCCTTTGACGGAAGGCATAGCCAAACCCTCAAGGCTATGGTC}$: PRAME Segment# : 5 Offset : 61 1st Codon : 1 A A F D G R H S Q T L K A M V Q A W P F T C L P L G V L M K Gene : PRAME Segment# : 6 : 76 1st Codon: 1 QAWPFTCLPLGVLMKGQHLHLETFKAVLDG : PRAME Segment# : 7 Offset : 91 $\texttt{G} \quad \texttt{Q} \quad \texttt{H} \quad \texttt{L} \quad \texttt{H} \quad \texttt{L} \quad \texttt{E} \quad \texttt{T} \quad \texttt{F} \quad \texttt{K} \quad \texttt{A} \quad \texttt{V} \cdot \texttt{L} \quad \texttt{D} \quad \texttt{G} \quad \texttt{L} \quad \texttt{D} \quad \texttt{V} \quad \texttt{L} \quad \texttt{L} \quad \texttt{A} \quad \texttt{Q} \quad \texttt{E} \quad \texttt{V} \quad \texttt{R} \quad \texttt{P} \quad \texttt{R} \quad \texttt{W} \quad \texttt{K}$ $\tt GGCCAACACCTCCACCTCGAGACATTCAAAGCCGTCCTGGATGGCCTCGACGTCCTGCTCGCCCCAAGAGGTCAGGCCTAGGAGATGGAAA$: PRAME Segment# : 8 Offset : 106 1st Codon : 1 L D V L L A Q E V R P R R W K L Q V L D L R K N S H Q D F W $\tt CTGGATGTGCTCCTGGCTCAGGAAGTGAGACCCAGAAGGTGGAAGCTCCAGGTCCTGGATCTGAGAAGAATAGCCATCAGGATTTCTGG$ Gene : PRAME Segment# : 9 Offset : 121 L Q V L D L R K N S H Q D F W T V W S G N R A S L Y S F P E $\tt CTGCAAGTGCTCGACCTCAGGAAAAACTCCCACCAAGACTTTTGGACAGTGTGGAGCGGAAACAGAGCCTCCCTGTATAGCTTTCCCGAA$ Gene : PRAME Segment# : 10 Offset : 136 1st Codon: 1
T V W S G N R A S L Y S F P E P E A A Q P M T K K R K V D G ACCGTCTGGTCCGGCAATAGGGCTAGCCTCTACTCCTTCCCTGAGCCTGAGCCTGACCCATGACCAAAAAGAGAAAAGGTCGACGA : PRAME Gene Segment# : 11 Offset : 151 1st Codon : 1 PEAAQPMTKKRKVDGLSTEAEQPFIPVEVL CCCGAAGCCGCTCAGCCTATGACAAAGGAAAAGGGAAAGTGGATGGCCTCAGCACAGAGGCTGAGCAACCCTTTATCCCTGTGGAAGTGCTC Gene ' : PRAME Segment# : 12 Offset : 166 1st Codon : 1 LSTEAEQPFIPVEVLVDLFLKEGACDELFS Gene : PRAME Segment# : 13 Offset 1st Codon : 1

Gene : PRAME Segment# : 14

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Offset : 196 1st Codon : 1 Y L I E K

Y L I E K V K R K K N V L R L C C K K L K I F A M P M Q D I TACCTCATCGAAAAAGGTCAAGAGAAAAAACGTCCTGAGACATT

Gene : PRAME Segment# : 15 Offset : 211 1st Codon : 1

C C K K L K I F A M P M Q D I K M I L K M V Q L D S I E D L TGCTGTAAGAACTGAAAATCTTTGCCATGCCATGCAGGACATCAAAATGATTCTGAAAATGGTCCAGCTCGACTCCATCGAAGACCTC

Gene : PRAME
Segment# : 16
Offset : 226
1st Codon : 1

K M I L K M V Q L D S I E D L E V T C T W K L P T L A K F S AAGATGATCCTCAAGATGCTGCAACTGGCATAGCATTGAGGATCTGGAAGTGACATGCACATGGAAACTGCCTACCCTCGCCAAATTCTCC

Gene : PRAME Segment# : 17 Offset : 241 1st Codon : 1

1st Codon: 1
E V T C T W K L P T L A K F S P Y L G Q M I N L R R L L L S
GAGGTCACCTGTACCTGGAAGCTCCCCACACTGGCTAAGTTTAGCCCTTACCTCGGCCAAATGATTAACCTCAGGAGACTGCTCCTGTCC

Gene : PRAME Segment# : 18 Offset : 256 1st Codon : 1

Gene : PRAME Segment# : 19 Offset : 271 1st Codon : 1

H I H A S S Y I S P E K E E Q Y I A Q F T S Q F L S L Q C L CACATTCACGCTAGCTCAGATTAGCCCTGCAAAGAGGGAAAGAGGAACAGTATATCGCTCAGTTTACCTCCCAGTTTCTGTCCCTGCAATGCCTC

Gene : PRAME Segment# : 20 Offset : 286 lst Codon : 1

Y I A Q F T S Q F L S L Q C L Q A L Y V D S L F F L R G R L TACATTGCCCAATTCACAAGCCAATTCCTCAGGCTCCAGTGTCTCTGCAAGCCCTCTACGTCGACTCCCTGTTTTTCCTCAGGGGAAGGCTC

Gene : PRAME Segment# : 21 Offset : 301 lst Codon : 1

Q A L Y V D S L F F L R G R L D Q L L R H V M N P L E T L S CAGGCTCTGTATGTGGATAGCCTCTTCTTCTGAGAGGCAGACTGGATCAGCTCCTGAGACACGTCATGAATCCCCTCGAGACACTGTCC

Gene : PRAME Segment# : 22 Offset : 316 1st Codon : 1

D Q L L R H V M N P L E T L S I T N C R L S E G D V M H L S GACCAACTGCTCAGGCATGATGAACCCTCTGGAAACCCTCAGCATTACCAATTGCAGACTGTCCGAGGGAACCGTCATGCATCTGTCC

Gene : PRAME
Segment# : 23
Offset : 331
1st Codon : 1

I T N C R L S E G D V M H L S Q S P S V S Q L S V L S L S G ATCACAAACTGTAGGCTCAGGCGAAGGGGGATGTGATGCACCTCAGCCAAAGCCCTAGCGTCAGCCAACTGTCCGTGCTCAGCCTCAGCGGA

Gene : PRAME Segment# : 24 Offset : 346 1st Codon : 1

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 $\begin{smallmatrix} Q & S & P & S & V & S & Q & L & S & V & L & S & L & S & G & V & M & L & T & D & V & S & P & E & P & L & Q & A & L & L \\ \end{smallmatrix}$: PRAME Segment# : 25 Offset : 361 1st Codon : 1 V M L T D V S P E P L Q A L L E R A S A T L Q D L V F D E C : PRAME Segment# : 26 Offset : 376 1st Codon : 1 ERASATLQDLVFDECGITDDQLLALLPSLS Gene : PRAME Segment# : 27 Offset : 391 1st Codon : 1 G I T D D Q L L A L L P S L S H C S Q L T T L S F Y G N S I GGCATTACCGATGACCAACTGCTCGCCCTCCTGCCTAGCCTCAGCCATTGCTCCCAGCTCACCACACTGTCCTTCTATGGCAATAGCATT : PRAME Segment# : 28 : 406 Offset 1st Codon : 1 H C S Q L T T L S F Y G N S I S I S A L Q S L L O H L I G L Gene : PRAME Segment# : 29 : 421 Offset S I S A L Q S L L Q H L I G L S N L T H V L Y P V P L E S Y AGCATTAGCGCTCTGCAAAGCCTCCTGCAACACCTCATCGGACTGTCCAACCTCACCCATGTGCTCTACCCTGTGCCTCTGGAAAGCTAT Gene : PRAME Segment# : 30 Offset : 436 1st Codon : 1 S N L T H V L Y P V P L E S Y E D I H G T L H L E R L A Y L AGCAATCTGACACGTCCTGTATCCCGTCCCCTCGAGTCCTACGAAGACATTCACGGAACCCTCCACCTCGAGAGACTGGCTTACCTC : PRAME Gene Segment# : 31 1st Codon : 1 E D I H G T L H L E R L A Y L H A R L R E L L C E L G R P S ${\tt GAGGATATCCATGGCACCTGCATCTGGAAAGGCTCGCCTATCTGCATGCCAGACTGAGAGAGCCTCCTGTGTGAGCTCGGCAGACCCTCC}$: PRAME Gene Segment# : 32 Offset : 466 1st Codon : 1 HARLRELLCELGRPSMVWLSANPCPHCGDR $\tt CACGCTAGGGTCAGGGAACTGCTGCGAACTGGGAAGGCCTAGCATGGTGTGGCTGTCCGCAATCCCTGTCCCCATTGCGGAGACAGA$: PRAME Gene Segment# : 33 Offset : 481 1st Codon : 1 M V W L S A N P C P H C G D R T F Y D P E P I L C P C F M P ATGGTCTGGCTCAGCGCTAACCCTTGCCCTCACTGTGGCGATAGGACATTCTATGACCCTGAGCCTATCCTCTGCCCTTACCCTTATGCCT Gene : PRAME Segment# : 34 1st Codon : 1 T F Y D P E P I L C P C F M P N A A ACCTTTACGATCCCGAACCCATTCTGTGTCCCTGTTTCATGCCCAATGCCGCT

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: TRP2IN2 Gene Segment# : 1 Offset 1st Codon: 1 A A L M E T H L S S K R Y T E E A G G F F P W L K V Y Y Y R GCCGCTCTGATGGAGACACACCTCAGCTCCAAGAGATACACAGAGGAAGCCGGAGGCTTTTTCCCTTGGCTCAAGGTCTACTATTACAGA : TRP2IN2 Segment# : 2 Offset : 16 1st Codon : 1 E A G G F F P W L K V Y Y Y R F V I G L R V W O W E V I S C ${\tt GAGGCTGGCGGATTCTTTCCCTGGCTGAAAGTGTATTACTATAGGTTTTGTGATTGGCCTCAGGGTCTGGCAATGGGAAGTGATTAGCTGT}$: TRP2IN2 Segment# : 3 Offset : 31 1st Codon : 1 F V I G L R V W Q W E V I S C K L I K R A T T R O P A A : NYNSOla Gene Segment# : 1 Offset : 1 1st Codon : 1 A A M Q A E G R G T G G S T G D A D G P G G P G I P D G P G GCCGCTATGCAAGCCGAAGGCAGAGGCACAGGCGGAAGCACAGGCGATGCCGATGGCCCTGGCGGACCCCGGAATCCCTGACGGACCCGGA : NYNSOla Segment# : 2 Offset : 16 1st Codon : 1 D A D G P G G P G I P D G P G G N A G G P G E A G A T G G R GACGCTGACGGACCCGGAGGCCCTGGCATTCCCGATGGCCCTGGCGGAAACGCTGGCGGACCCGGAGAGGCTGGCGCTACCGGAGGCAGA Gene : NYNSOla Segment# : 3 Offset : 31 G N A G G P G E A G A T G G R G P R G A G A A R A S G P G G : NYNSOla Segment# : 4 Offset : 46 1st Codon : 1 G P R G A G A A R A S G P G G G A P R G P H G G A A S G L N GGCCCTAGGGGAGCCGGAGCCGCTAGGGCTAGCGGACCCGGAGGCGGAGCCCCTAGGGGGACCCCATGGCGGAGCCGCTAGCGGACTGAAT : NYNSO1a Gene Segment# : 5 Offset : 61 1st Codon : 1 G A P R G P H G G A A S G L N G C C R C G A R G P E S R L L ${\tt GGCGCTCCCAGAGGCCCTCACGGAGGCGCTGCCTCCAGGGATGCTGTAGGTGTGGCGCTAGGGGACCCGAAAGCAGACTGCTC}$: NYNSOla Segment# : 6 Offset : 76 1st Codon : 1 G C C R C G A R G P E S R L L E F Y L A M P F A T P M E A E ${\tt GGCTGTTGCAGATGCGGAGCCAGAGGCCCTGAGTCCAGGCTCCTGGAATTCTATCTGGCTATGCCTTTCGCTACCCCTATGGAAGCCGAA}$ Gene : NYNSOla Segment# : 7 Offset : 91 1st Codon : 1 $\hbox{\tt E F Y L A M P F A T P M E A E L A R R S L A Q D A P P L P V}$ GAGTTTTACCTCGCCATGCCCTTTGCCACACCCATGGAGGCTGAGCTCGCCAGAAGGTCCCTGGCTCAGGATGCCCCTCCCCTCCCCGTC : NYNSOla

Gene

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Segment# : 8 Offset : 106 1st Codon : 1 L A R R S L A Q D A P P L P V P G V L L K E F T V S G N I L $\tt CTGGCTAGGAGAAGCCTCGCCCAAGACGCTCCCCCTCTGCCTGGCGTGCTCCTGAGGAATTCACAGTGTCCGGCAATATCCTC$: NYNSOla Segment# : 9 Offset : 121 1st Codon : 1 P G V L L K E F T V S G N I L T I R L T A A D H R O L O L S CCCGGAGTGCTCCTGAAAGAGTTTACCGTCAGCGGAAACATTCTGACAATCAGACTGACAGCCGCTGACCATAGGCAACTGCAACTGTCC Gene : NYNSOla Segment# : 10 Offset : 136 1st Codon : 1 TIRLTAADHRQLQLSISSCLQQLSLLMWIT : NYNSOla Segment# : 11 Offset : 151 1st Codon : 1 I S S C L Q Q L S L L M W I T Q C F L P V F L A Q P P S G Q Gene : NYNSOla Segment# : 12 Offset : 166 1st Codon: 1 QCFLPVFLAQPPSGQRRAA CAGTGTTTCCTCCCCGTCTTCCTCGCCCAACCCCCTAGCGGACAGAGAGGGCTGCC : NYNSOlb Gene Segment# : 1 Offset 1st Codon : 1 A A M L M A Q E A L A F L M A Q G A M L A A O E R R V P R A $\tt GCCGCTATGCTCATGGCTCAGGAAGCCCTCGCCTTTCTGATGGCCCAAGGCGCTATGCTCGCCGCTCAGGAAAGGAGAGTGCCTAGGGCT$ Gene : NYNSO1b Segment# : 2 Offset : 16 1st Codon : 1 CAGGGAGCCATGCTGGCTGCCCAAGAGAGAGAGGGTCCCCAGAGCCGCTGAGGTCCCCGGAGCCCAAGGCCAACAGGGACCCAGAGGCAGA Gene : NYNSO1b Segment# : 3 Offset : 31 A E V P G A Q G Q Q G P R G R E E A P R G V R M A A R L O G GCCGAAGTGCCTCAGGGACAGCAAGGCCCTAGGGGAAGGGGAAGAGGCTCCCAGAGGCGTCAGGATGGCCGCTAGGCTCCAGGGA : NYNSO1b Gene Segment# : 4 Offset : 46 1st Codon : 1 E E A P R G V R M A A R L Q G A A GAGGAAGCCCCTAGGGGAGTGAGAATGGCTGCCAGACTGCAAGGCGCTGCC Gene : LAGE1 Segment# : 1 Offset Gene : LAGE1 Segment# : 2

Figure 27 (Cont)

Offset

: 16

194/216

1st Codon : 1 GACGCTGACGGACCCGGAGGCCCTGGCATTCCCGATGGCCCTGGCGGAAACGCTGGCGGACCCGGAGAGGCTGCCGCATCCGGAGGCAGA Gene : LAGE1 Segment# : 3 : 31 1st Codon: 1 G N A G G P G E A G A T G G R G P R G A G A A R A S G P R G : LAGE1 Segment# : 4 Offset : 46 1st Codon : 1 $\texttt{G} \ \ \texttt{P} \ \ \texttt{R} \ \ \texttt{G} \ \ \texttt{A} \ \ \texttt{A} \ \ \texttt{A} \ \ \texttt{S} \ \ \texttt{G} \ \ \texttt{P} \ \ \texttt{R} \ \ \texttt{G} \ \ \texttt{G} \ \ \texttt{P} \ \ \texttt{R} \ \ \texttt{G} \ \ \texttt{P} \ \ \texttt{H} \ \ \texttt{G} \ \ \texttt{G} \ \ \texttt{A} \ \ \texttt{A} \ \ \texttt{S} \ \ \texttt{A} \ \ \texttt{Q} \ \ \texttt{D}$ $\tt GGCCCTAGGGGAGCCGGAGCCGCTAGGGGACCCAGAGGGGGAGCCCCTAGGGGAGCCCCTAGGGGAGCCGCTAGCGCTCAGGAT$: LAGE1 Segment# : 5 Offset : 61 1st Codon : 1 G A P R G P H G G A A S A Q D G R C P C G A R R P D S R L L GGCGCTCCCAGAGGCCCTCACGGAGGCGCTGCCTCCGCCCAAGACGGAAGGTGTCCCTGTGGCGCTAGGAGACCCGATAGCAGACTGCTC Gene : LAGE1 Segment# : 6 Offset : 76 1st Codon : 1 G R C P C G A R P D S R L L Q L H I T M P F S S P M E A E GGCAGATGCCCTTGCGGAGCCAGAAGGCCTGACTCCAGGCTCCTGCAACTGCATATCACAATGCCTTTCTCCAGCCCTATGGAAGCCGAA : LAGE1 Segment# : 7 Offset : 91 1st Codon : 1 $\begin{smallmatrix} Q & L & H & I & T & M & P & F & S & S & P & M & E & A & E & L & V & R & R & I & L & S & R & D & A & P & L & P & R \end{smallmatrix}$ Gene : LAGE1 Segment# : 8 Offset : 106 1st Codon : 1 L V R R I L S R D A A P L P R P G A V L K D F T V S G N L L $\tt CTGGTCAGGAGAATCCTCAGCAGGAGACGCTGCCCCTCTGCCTAGGCCTGGCGCTGTGCTCAAGGATTTCACAGTGTCCGGCAATCTGCTC$ Segment# : 9 Offset : 121 1st Codon : 1 P G A V L K D F T V S G N L L F I R L T A A D H R Q L Q L S CCCGGAGCCGTCCTGAAAGACTTTACCGTCAGCGGAAACCTCCTGTTTATCAGACTGACAGCCGCTGACCATAGGCAACTGCAACTGTCC Gene : LAGE1 Segment# : 10 Offset : 136 1st Codon : 1 FIRLTAADHRQLQLSISSCLQQLSLLMWIT : LAGE1 Segment# : 11 : 151 Offset 1st Codon : 1 ISSCLQQLSLLMWITQCFLPVFLAQAPSGQ : LAGE1 Gene Segment# : 12 Offset : 166 1st Codon : 1 QCFLPVFLAQAPSGQRRAA

195/216

CAGTGTTTCCTCCCCGTCTTCCTCGCCCAAGCCCCTAGCGGACAGAGAAGGGCTGCC

Segments in scrambled order:

MAGE-1 #15

A P E E E I W E E L S V M E V Y D G R E H S A Y G E P R K L GCCCCTGAGGAAGAGTTTGGGAAGAGCTCAGGAAAGGCTC

MAGE-1 #4

PRAME #10

MAGE-3 #14

PRAME #9

L Q $^{
m V}$ L D L R K N S H Q D F W T V W S G N R A S L Y S F P E CTGCAAGTGCTCGACCTCAGGAAAAACTCCCACCAAGACTTTTGGACAGTGTGGAGCGGAAACAGAGCCTCCCTGTATAGCTTTCCCGAA

PRAME #8

NYNSO1b #2

PRAME #24

Q S P S V S Q L S V L S L S G V M L T D V S P E P L Q A L L CAGTCCCCTCCGTGTCCAGCTCAGCGTCCTGTCCGGCGTCATGCTCACCGATGTGTCCCCGAACCCTTCCAGGCTCTGCTC

MAGE-1 #17

MAGE-1 #6

BAGE #1

A A M A A R A V F L A L S A Q L L Q A R L M K E E S P V V S GCCGCTATGGCTGCCAGAGCCAGACTGATGAAGGAAGAGTCCCCGGTCGTGTCC

PRAME #34

T F Y D P E P I L C P C F M P N A A ACCTTTTACGATCCCGAACCCATTCTGTGTCCCTGTTTCATGCCCAATGCCGCT

MAGE-3 #12

GAGE-1 #2

TRP2IN2 #2

E A G G F F P W L K V Y Y Y R F V I G L R V W Q W E V I S C GAGGCTGGCGATTCTTTCCCTGGCTGAAAGTGTATTACTATAGGTTTGTGATTGGCCTCAGGGTCTGGCAATGGGAAGTGATTAGCTGT

PRAME #1

A A M E R R R L W G S I Q S R Y I S M S V W T S P R R L V E GCCGCTATGGAAAGGAGAAGGCTCTGGGAAGGATCAGTCCAGGTATATCTCCATGTCCGTGTGGACCTCCCCCAGAAGGCTCGTGGAA

TRP2IN2 #1

A A L M E T H L S S K R Y T E E A G G F F P W L K V Y Y Y R GCCGCTCTGATGGAGACACACCTCAGGAGATACACAGAGGAAGCCGGAGGCTTTTTCCCTTGGCTCAAGGTCTACTACTACAGA

196/216

MAGE-1 #1

A A M S L E Q R S L H C K P E E A L E A Q Q E A L G L V C V GCCGCTATGTCCCTGGAACAGAGGCTCCACTGTAAGCCTGAGGAAGCCTCAGGAAGAGGCTCTGGGACTGGTCTGCGTC

MAGE-1 #:

Q A A T S S S P L V L G T L E E V P T A G S T D P P Q S P CAGGCTGCCACAGGCTCCCCAAGGCCTCCCCAAAGCCCTACAGCCCACAGCCGGAAGCACAGACCCTCCCCAAAGCCCT

PRAME #4

A L E L L P R E L F P P L F M A A F D G R H S Q T L K A M V GCCCTCGAGCTCCTGCCTAGGGAACCCTCAAGGCTATGGTC

MAGE-3 #16

E L S V L E V F E G R E D S I L G D P K K L L T Q H F V Q E GAGCTCAGCGTCCTGGAAAAGCTCCTGACACAGCATTTCGTCCAGGAA

MAGE-1 #11

. MAGE-3 #5

P D P P Q S P Q G A S S L P T T M N Y P L W S Q S Y E D S S CCCGATCCCCTCAGTCCCCCAAGGCGCTAGCTCCCTACCACAATGAATTACCCTCTGTGGAGCCAAAGCTATGAGATAGCTCC

LAGE1 #1

NYNSOla #12

Q C F L P V F L A Q P P S G Q R R A A CAGTGTTTCCTCCCCGTCTTCCTCGCCCAACCCCCTAGCGGACAGAGAAGGGCTGCC

qp100In4 #2

T W G E G L P S Q P I I H T C V Y F F L P D H L S F G R P F ACCTGGGGCGAAGGCCTCCCCAGCCTATCATCACACATGCGTCTACTTTTTCCTCCCCGATCACCTCAGCTTTGGCAGACCCTTT

MAGE-1 #7

S T S C I L E S L F R A V I T K K V A D L V G F L L L K Y R AGCACAAGCTGTATCCTCGAGTCCCTGTTTAGGGCTGTGATTACCAAAAAGGTCGCCGATCTGGTCGGCTTTCTGCTCCTGAAATACAGA

NYNSO1a #1

GAGE-1 #7

D G P D G Q E M D P P N P E E V K T P E E E M R S H Y V A Q GACGGACCCGATGGCCAAGAGATGGACACCTCCCAATCCCGAAGAGGTCAAGACACCCGAAGAGGAAATGAGAAGCCATTACGTCGCCCAA

NYNSOla #11

ISSCLQQLSLLMWITQCFLPVFLAQPPSGQATCTCCAGCTGTGTTTCTGGCTCAGCCTCCTCCGGCCAA

PRAME #26

E R A S A T L Q D L V F D E C G I T D D Q L L A L L P S L S GAGAGAGCCTCCGCCACACGACCTCCTGTCTTGACGAATGCGGAATCACAGACGATCAGCTCCTGGCTCTGCTCCCTGTCC

MAGE-3 #17

MAGE-1 #2

E A L E A Q Q E A L G L V C V Q A A T S S S P L V L G T L GAGGCTCTGGAAGCCCTACCTCCAGCCCTCTGGTCCTGGGAACCCTC GGGAACCCTC

NYNSOla #7

NYNSO1b #4

E E A P R G V R M A A R L Q G A A GAGGAAGCCCCTAGGGGAGTGAGAATGGCTGCCAGACTGCAAGGCGCTGCC

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BAGE #3

W R L E P E D G T A L C F I F A A TGGAGACTGGAACCCGAAGACGGAACCGCTCTGTGTTTCATTTTCGCTGCC

GAGE-1 #3

E Q F S D E V E P A T P E E G E P A T Q R Q D P A A A Q E G GAGCAATTCTCCGACGAAGTGGAACCCGCTACCCTAGGGAAGGCCAAGAGGCAAGCCCTGCCGCTGCCCAAGAGGGA

MAGE-3 #6

T M N Y P L W S Q S Y E D S S N Q E E E G P S T F P D L E S ACCATGAACTATCCCTCTGGTCCCAGTCCTAGGAAGACTCCAGGAAGAGGAAGAGGGAAGAGGCCCTAGCACATTCCCTGACCTCGAGTCC

MAGE-3 #7

NQEEEGPSTFPDLESEFQAALSRKVAELVH

PRAME #13

NYNSOla #10

MAGE-3 #1

NYNSOla #2

D A D G P G G P G I P D G P G G N A G G P G E A G A T G G R GACGCTGACGGAGGCCCTGGCGTACCGGAGGCAGAGGCAGAGAGGCCTGGCGGAGAGGCCTGGCGGAGAGGCAGAGAGGCTGGCGCAGCAGAGAGGCAGA

MAGE-3 #19

Y E F L W G P R A L V E T S Y V K V L H H M V K I S G G P H TACGAATTCCTCTGGGGAACCCCTCGTGGAAACCTCCTACGTCAAGGTCCTGCATCACATGGTGAAAATCTCCGGCGGACCCCAT

PRAME #23

I T N C R L S E G D V M H L S Q S P S V S Q L S V L S L S G ATCACAAACTGTAGGCTCAGCGAAGGCGATGTGATGCACCTCAGCCAAAGCCCTAGCGTCAGCCAACTGTCCGTGCTCAGCCTCAGCGGA

MAGE-3 #18

N Y L E Y R Q V P G S D P A C Y E F L W G P R A L V E T S Y AACTATCTGGAATACAGACAGGTCCCCGGAAGCGATCCCGCTTGCTATGAGTTTCTGTGGGGCCCTAGGGCTCTGGTCGAGACAGCTAT

MAGE-3 #11

PRAME #21

Q A L Y V D S L F F L R G R L D Q L L R H V M N P L E T L S CAGGCTCTGTATGTGGATAGCCTCTTTTTTTGAGAGGCAGACTGGATCAGCTCCTGAGACACGTCATGAGATCCCCTCGAGACACTGTCC

PRAME #20

Y I A Q F T S Q F L S L Q C L Q A L Y V D S L F F L R G R L TACATTGCCCAATTCACAAGCCAATTCCTCAGGGGAAGGCTCTGCAAGCCCTCTACGTCGACTCCCTGTTTTTCCTCAGGGGAAGGCTC

PRAME #

G Q H L H L E T F K A V L D G L D V L L A Q E V R P R R W K GGCCAACACCTCCACCTCGAGACATTCAAAGCCGTCCTGGATGGCCTCGACGTCCTGCTCGCCCAAGAGGTCAGGCCTAGGAGATGGAAA

LAGE1 #10

FIRLT A A D H R Q L Q L S I S S C L Q Q L S L L M W I T TTCATTAGGCTCACCGCTGCCGATCACAGACAGCTCCAGCTCAGCATTAGCTCCTGCTCCAGCAACTGTCCTGCTCATGTGGATCACA

PRAME #15

NYNSOla #5

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MAGE-1 #8

K K V A D L V G F L L K Y R A R E P V T K A E M L E S V I AAGAAAGTGGCTGACCTCGTGGGATTCCTCCTGCTCAAGTATAGGGCTAGGGAACCCGTCACCAAAGCCGAAATGCTCGAGTCCGTGATT

MAGE-1 #13

PRAME #29

MAGE-3 #15

PRAME #22

D Q L L R H V M N P L E T L S I T N C R L S E G D V M H L S GACCAACTGCTCAGGCATGATGAACCCTCTGGAAACCCTCAGCATTACCAATTGCAGACTGTCCGAGGGAGACGTCATGCATCTGTCC

MAGE-1 #19

PRAME #30

S N L T H V L Y P V P L E S Y E D I H G T L H L E R L A Y L AGCAATCTGACACACGTCCTGTATCCCGTCCCCTCGAGTCCTACGAGAGACATTCACGGAACCCTCCACCTCGAGAGACTGGCTTACCTC

NYNSOlb #1

A A M L M A Q E A L A F L M A Q G A M L A A Q E R R V P R A GCCGCTATGCTCATGGCTCAGGAAAGGAGTGCCTAGGGCT

MAGE-1 #10

K N Y K H C F P E I F G K A S E S L Q L V F G I D V K E A D AAGAATTACAAACACTGTTTCCCTGAGATTTCCGGAAAGGCTAGCGAAAGCCTCCAGCTCGTGTTTGGCATTGACGTCAAGGAAGCCGAT

MAGE-3 #4

T L V E V T L G E V P A A E S P D P P Q S P Q G A S S L P T ACCCTCGTGGAAGTGACACTGGGAGAGGTCCCCGCTGCCGAAAGCCCTCCCAAAGCCCTCAGGGAGCCTCCCGCACA

PRAME #32

HARLRELLCELGRPSMVWLSANPCPHCGDRCCCACCCATGCGGAACTGCGGAACTGCGGAACTGCGGAACTGCGGAACTGCGGAACTGCGGAACAGA

PRAME #25

V M L T D V S P E P L Q A L L E R A S A T L Q D L V F D E C GTGATGCTGACAGACGTCAGCCTCTGGAAGCCCTCCTGGAAGGGCTAGCGCTACCCTCCAGGATCTTGGATGAGTGT

GAGE-1 #5

E D E G A S A G Q G P K P E A D S Q E Q G H P Q T G C E C E GAGGATGAGGGAGCCTCCGCCGAACCGGATGCGAACCCGAAGCCGATAGCCAAGAGCAAGGCCATCCCCAAACCGGATGCGAATGCGAA

MAGE-3 #10

EMLGSVVGNWQYFFPVIFSKASSSLQLVFGGAGATGCTCTGGGAAGCCTCCAGCTCCTGCAACTGGTCTTCGGA

GAGE-1 #1

A A M S W R G R S T Y R P R P R R Y V E P P E M I G P M R P GCCGCTATGTCCTGGAGGGGAGGCAGAAGCATACAGACCCAGAAGGTATGTGGAACCCCTGAGATGATCGGACCCATGAGGCCT

PRAME #2

Y I S M S V W T S P R R L V E L A G Q S L L K D E A L A I A TACATTAGCATGAGCGTCTGGACAGCCCTAGGAGACTGGTCGAGGACAGTCCCTGCTCAAGGATGAGCTCTGGCTATCGCT

MAGE-1 #16

LAGEL #12

199/216

MAGE-3 #20

LAGE1 #7

Q L H I T M P F S S P M E A E L V R R I L S R D A A P L P R CAGCTCCACATTACCATGCCCTTTAGCTCCCCATGGAGGCTCGAGAAGGATTCTGTCCAGGGATGCCGCTCCCCTCCCCAGA

NYNSOla #9

P G V L L K E F T V S G N I L T I R L T A A D H R Q L Q L S CCCGGAGTGCTCCTGAAAGAGTTTACCGTCAGCGGAAACATTCTGACAATCAGACTGACAGCCGCTGACCATAGGCAACTGCAACTGTCC

PRAME #16

K M I L K M V Q L D S I E D L E V T C T W K L P T L A K F S AAGATGATCCTCAAGATGGTGCAACTGGATAGCATTGAGGATCTGGAAGTGACATGGAAACTGCCTACCCTCGCCAAATTCTCC

MAGE-1 #14

F L I I V L V M I A M E G G H A P E E E I W E E L S V M E V TTCCTCATCATCGTGGTGGTGGTGGTGGTGGTGGGGGGACACGCTCCCGAAGAGGAAATCTGGGAGGAACTGTCCGTGATGGAGGGTC

PRAME #17

E V T C T W K L P T L A K F S P Y L G Q M I N L R R L L L S GAGGTCACCTGTACCTGGAAGCTCCCCACACTGGCTAAGTTTAGCCCTTACCTCGGCCAAATGATTAACCTCAGGAGACTGCTCCTGTCC

MAGE-3 #2

E G L E A R G E A L G L V G A Q A P A T E E Q E A A S S S GAGGGACTGGAAGCCCAAGGCCAAGCCCCAAGCCCCAAGAGGAACAGGAAGAGCCGCTAGCTCCAGCTCC

MAGE-3 #21

PRAME #19

H I H A S S Y I S P E K E E Q Y I A Q F T S Q F L S L Q C L CACATTCACGCTAGCTCCAGTTAGCCCTGCAAAGAGAAGAGGAACAGTATATCGCTCAGTTTACCTCCCAGTTTCTGTCCCTGCAATGCCTC

NYNSOla #3

G N A G G P G E A G A T G G R G P R G A G A R A S G P G G GGCAATGCCGGAGGCCTGGCGAAGCCGAAGGCGAAGGCGAAGGCGAAGGCGCAGAGGCCTCCGGCCCTGGCGGA

NYNSOla #4

G P R G A G A A R A S G P G G G A P R G P H G G A A S G L N GGCCCTAGGGGAGCCGCTAGGGGCTAGCGGACCGGAGCCCCTAGGGGAGCCCCATGGCGGAGCCGCTAGCGGACCGGAGCCGCATGAAT

MAGE-1 #5

NYNSOla #8

LARRSLAQDAPPLPVPGVLLKEFTVSGNILCTGGCTAGGAGAGCCTCGCCCAAGACGCTCCCCCTCTGCCTGGCGTCCTCCAAGGAATTCACAGTGTCCGGCAATATCCTC

PRAME #5

A A F D G R H S Q T L K A M V Q A W P F T C L P L G V L M K GCCGCTTTCGATGCCAGACACTCCAGACACTGAAAGCCATGGTGCAGCCCTTTACCTGTCTGCCTCTGGGAGTGCTCATGAAA

MAGE-1 #20

PRAME #27

G I T D D Q L L A L L P S L S H C S Q L T T L S F Y G N S I GGCATTACCGATGACCAACTGCTCCTCCTGCCTAGCCTCAGCCATTGCTCCCAGCTCACCACACTGTCCTTCTATGGCAATAGCATT

GAGE~1 #8

V K T P E E E M R S H Y V A Q T G I L W L L M N N C F L N L GTGAAAACCCCTGAGGAAGAGAGAGAGGTCCCACTATGTGGCTCAGACAGGCATTCTGTGGCTGAGTAAAACCGTTTCCTCAACCTC

LAGE1 #11

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PRAME #14

Y L I E K V K R K K N V L R L C C K K L K I F A M P M Q D I TACCTCATCGAAAAAGGTCAAGAGAAAAAACGTCCTGAGACTGTGTGCAAAAAGGTCAAGAGTTTTCGCTATGCCTATGCAAGAGACATT

MAGE-1 #9

A R E P V T K A E M L E S V I K N Y K H C F P E I F G K A S GCCAGAGAGCCTGTGACAAAGGCTGAGATGCTTGGCAAAGCCTCC

LAGE1 #8

L V R R I L S R D A A P L P R P G A V L K D F T V S G N L L CTGGTCAGGAGAATCCTCAGCAGAGACGCTGCCCCTCTGCCTAGGCCTGCCCTGTGCTCAAGGATTTCACAGTGTCCGGCAATCTGCTC

PRAME #28

H C S Q L T T L S F Y G N S I S I S A L Q S L L Q H L I G L CACTGTAGCCAACCCTCAGCTTTTACGGAAACTCCATCTCCATCTCCGCCCTCCAGTCCTGCTCCAGCCATCTGATTGGCCTC

PRAME #33

M V W L S A N P C P H C G D R T F Y D P E P I L C P C F M P ATGGTCTGGCGCTAACCCTTGCCTCACTGTGGCGATAGGACATTCTATGACCCTGAGCCTATCCTCTGCCCTTGCTTTATGCCT

qp100In4 #1

A A S W S Q K R S F V Y V W K T W G E G L P S Q P I I H T C GCCGCTAGCTGGAGCCAAAAGAGAAGCTTTGTGTATGTGTGGAAGACATGGGGAGAGGGACTGCCTAGCCAACCCATTATCCATACCTGT

BAGE #2

L L Q A R L M K E E S P V V S W R L E P E D G T A L C F I F CTGCTCCAGGCTAGGCTCAGGAAAGAGGAAAGCCCTGTGGTCAGCTGAGGGCTCGAGGATGGCACAGCCCTCTGCTTTATCTTT

qp100In4 #3

V Y F F L P D H L S F G R P F H L N F C D F L A A GTGTATTTCTTGCCTGACCATCTGGCAGGCCTTTCCATCTGAATTTCTTGGCTTCCCTTCGCTGCC

PRAME #18

MAGE-3 #3

PRAME #6

Q A W P F T C L P L G V L M K G Q H L H L E T F K A V L D G CAGGCTTGGCCTTTCACATGCCTCCCCCTCGGCGTCCTGATGAAGGGACACCTCTGCATCTGGAAACCTTTAAGGCTGTGCTCGACGGA

PRAME #12

NYNSOlb #3

LAGE1 #5

G A P R G P H G G A A S A Q D G R C P C G A R R P D S R L L GGCGCTCCCAGAGGCCCTCCCGAGAGGCGCTCCCAAGACGCGAAGGTGTCCCTGTGGCGCTAGGAGACCCGATAGCAGACTGCTC

LAGE1 #4

G P R G A G A A R A S G P R G G A P R G P H G G A A S A Q D GGCCCTAGGGGAGCCGTAGGGCTAGGGCTAGGGGTCAGGAT

PRAME #3

LAGQSLLKDEALAIAALELLPRELFPPLFM CTGGCTGGCCAAAGCCTCTGAAAGACGAAGCCCTCGCCATTGCCGCTCTGGAACTGCTCCCAGAGAGGCTCTTCCCTCCTCTCATG

GAGE-1 #4

E P A T Q R Q D P A A A Q E G E D E G A S A G Q G P K P E A GAGCCTGCCACACAGAGACAGGAAGACGCAAGACGCAAGGCCCTAAGCCTGAGGCT

PRAME #11

P E A A Q P M T K K R K V D G L S T E A E Q P F I P V E V L CCCGAAGCCGCTCAGCCATGACAAAAAAAAAAGGAAAGTGGATGGCTCAGCACAGAGGCTGAGCAACCCTTTATCCCTGTGGAAGTGCTC .

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LAGE1 #6

GRCPCGARRPDSRLLOLLHITMPFSSPMEAEGGCAGAGATGCCTTTCTCCAGCCTATGGAAGCCGAA

LAGE1 #:

P G A V L K D F T V S G N L L F I R L T A A D H R Q L Q L S CCCGGAGCCGTCCTGAAAGACTTTACCGTCAGCGAAACCTCCTGTTTATCAGACTGACAGCCGCTGACCATAGGCAACTGCAACTGTCC

PRAME #31

E D I H G T L H L E R L A Y L H A R L R E L L C E L G R P S GAGGATATCCATGGCACCTCTGTGTGAGCTCGGCAGACCTCC

GAGE-1 #6

D S Q E Q G H P Q T G C E C E D G P D G Q E M D P P N P E E GACTCCCAGGAACAGGACACCCTCAGACAGGCTGTGAGGTGTGAGGATGGCCCTGACGGACAGGAAATGGATCCCCTAACCCTGAGGAA

TRP2IN2 #3

F V I G L R V W Q W E V I S C K L I K R A T T R Q P A A TTCGTCATCGGACTGGGAGGTGGGAGGTCATCTCCTGCAAACTGATTAAGAGAGCCACAACCAGACAGCCTGCCGCT

LAGE1 #2

MAGE-1 #12

MAGE-3 #9

GAGE-1 #9

T G I L W L L M N N C F L N L S P R K P A A ACCGGAATCCTCTGGCTCCTGATGAACAATTGCTTTCTGAATCTGTCCCCCAGAAAGCCTGCCGCT

MAGE-3 #8

EFQAALSRKVAELVHFLLLKYRAREPVTKA GAGTTTCAGGCTGCCCTCAGCAGAAGGTCGCCGAACTGGTCCACTTTCTGCTCCTGAAATACAGAGCCAGAGAGCCTGTGACAAAGGCT

MAGE-1 #18

NYNSO1a #6

G C C R C G A R G P E S R L L E F Y L A M P F A T P M E A E GGCTGTTGCAGATGCGGAGCCGAGGCCCTGAGTCCAGGCTCCTGGAATTCTATCTGGCTATGCCTTTCGCTACCCCTATGGAAGCCGAA

MAGE-3 #13

A T C L G L S Y D G L L G D N Q I M P K A G L L I I V L A I GCCACATGCCTCGGCCTCAGCTATGACGGACTGCTCGGCGATAACCAAATCATGCCCCAAAGCCGGACTGCTCATCATTGTGCTCGCCATT

LAGE1 #3

Artificial Protein:

APEEEIWELSVMEVYDGREHSAYGEPRKLEEVPTAGSTDPPQSPQGASAFPTTINFTRQTVWSGNRASLYSFPEPAAQPMTKKRKVDGQIMPKAGL
LIIVLAIIAREGDCAPEEKIWELQVLDLRKNSHQDFWTVWSGNRASLYSFPELDVLLAQEVRPRWKLQVLDLRKNSHQDFWQGAMLAAQERRVPRAA
EVPGAQGQQGPRGRQSPSVSQLSVLSLSGVMLTDVSPBFLQALLLTQDLVQEKYLEYRQVPDSDPARYEFLWGPRQPSEGSSREEEGPSTSCILESL
FRAVITAAMAARAVFLALSAQLLQARLMKEESPVVSTFYDPEPILCPCFMPNAAIELMEVDPJGHLYIFATCLGLSYDGLLGDNRRYVEPPEMIGPMR
PEQFSDEVEPATPEEGEAGGFFPWLKVYYYRFVIGLRVWQWEVISCAAMERRRLWGSIQSRYISMSVWTSPRRLVEAALMETHLSSKRYTEEAGGFFP
WLKVYYYRAAMSLEQRSLHCKPEEALEAQQEALGLVCVQAATSSSSPLVLGTLEEVPTAGSTDPPQSPALELLPRELFPPLFMAAFDGRHSQTLKAMV
ELSVLEVFEGREDSILGDPKKLLTQHFVQEESLQLVFGIDVKEADPTGHSYVLVTCLGLSPDPPQSPQGASSLPTTMNYPLWSQSYEDSSAAMQAEGQ
GTGGSTGDADGPGGPGIPDGPGQCFLPVFLAQPPSGQRRAATWGEGLPSQPIIHTCVYFFLPDHLSFGRPFSTSCILESLFRAVITKKVADLVGFLLL
KYRAAMQAEGRGTGGSTGDADGPGGPGIPDGPGDGDGDGDGQEMDPPNPEEVKTPEEEMRSHYVAQISSCLQQLSLLMWITQCFLPVFLAQPPSGQERASA
TLQDLVFDECGITDDQLLALLPSLSGDPKKLLTQHFVQENYLEYRQVPGSDPACEALEAQQEALGLVCVQAATSSSSPLVLGTLEFYLAMPFATPME
AELARRSLAQDAPPLPVEEAPRGVRMAARLQGAAWRLEPEDGTALCFIFAAEQFSDEVEPATPEEGEPATQRQDPAAAQETMNYPLWSQSYEDSSNQ
EEEGPSTFPDLESNQEEEGPSTFPDLESEFQAALSRKVAELVHVUDLFLKEGACDELFSYLIEKVKRKKNVLRLTIRLTAADHRQLGLSISSCLQQLSL
LMWITAAMPLEQRSQHCKPEEGLEARGEALGLVGADADGPGGPGIPDGPGGNAGGPGEAGATGGRYEFFLWGPRALVETSYVKVLHHMVKISGGPHITN
CRLSEGDVMHLSQSPSVSQLSVLSLSGNYLEYRQVPGSDPACYEFLWGPRALVETSYVIFSKASSSLQLVFGIELMEVDPIGHLYIFQALYVDSLFFL

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 $\tt RGRLDQLLRHVMNPLETLSYIAQFTSQFLSLQCLQALYVDSLFFLRGRLGQHLHLETFKAVLDGLDVLLAQEVRPRRWKFIRLTAADHRQLQLSISSC$ LOOLSLLMWITCCKKLKIFAMPMODIKMILKMVOLDSIEDLGAPRGPHGGAASGLNGCCRCGARGPESRLLKKVADLVGFLLLKYRAREPVTKAEMLE SVIYDGLLGDNQIMPKTGFLIIVLVMIAMEGGHSISALQSLLQHLIGLSNLTHVLYPVPLESYIAREGDCAPEEKIWEELSVLEVFEGREDSIDQLLR ${\tt HVMNPLETLSITNCRLSEGDVMHLSRALAETSYVKVLEYVIKVSARVRFFFPSLRSNLTHVLYPVPLESYEDIHGTLHLERLAYLAAMLMAQEALAFL}$ ${\tt MAQGAMLAAQERRVPRAKNYKHCFPEIFGKASESLQLVFGIDVKEADTLVEVTLGEVPAAESPDPPQSPQGASSLPTHARLRELLCELGRPSMVWLSA$ $\tt NPCPHCGDRVMLTDVSPEPLQALLERASATLQDLVFDECEDEGASAGQGPKPEADSQEQGHPQTGCECEEMLGSVVGNWQYFFPVIFSKASSSLQLVFIPLOFF AND STATEMENT OF STATEMENT$ GAAMSWRGRSTYRPRPRRYVEPPEMIGPMRPYISMSVWTSPRRLVELAGQSLLKDEALAIAYDGREHSAYGEPRKLLTQDLVQEKYLEYRQQCFLPVF ${\tt LAQAPSGQRRAAVKVLHHMVKISGGPHISYPPLHEWVLREGEQLHITMPFSSPMEAELVRRILSRDAAPLPRPGVLLKEFTVSGNILTIRLTAADHRQ}$ LQLSKMILKMVQLDSIEDLEVTCTWKLPTLAKFSFLIIVLVMIAMEGGHAPEEEIWEELSVMEVEVTCTWKLPTLAKFSPYLGQMINLRRLLLSEGLE ARGEALGLVGAQAPATEEQEAASSSSISYPPLHEWVLREGEEAAHIHASSYISPEKEEQYIAQFTSQFLSLQCLGNAGGPGEAGATGGRGPRGAGAAR ASGPGGGPRGAGAARASGPGGGAPRGPHGGAASGLNQGASAFPTTINFTRQRQPSEGSSSREEEGPLARRSLAQDAPPLPVPGVLLKEFTVSGNILAAFDGRHSOTLKAMVQAWPFTCLPLGVLMKIKVSARVRFFFPSLREAALREEEEGVAAGITDDQLLALLPSLSHCSQLTTLSFYGNSIVKTPEEEMRSHY VAQTGILWLIMNINCFLINLISSCLQQLSLLMWITQCFLPVFLAQAPSGQYLIEKVKRKKNVLRLCCKKLKIFAMPMQDIAREPVTKAEMLESVIKNYKH CFPEIFGKASLVRRILSRDAAPLPRPGAVLKDFTVSGNLLHCSQLTTLSFYGNSISISALQSLLQHLIGLMVWLSANPCPHCGDRTFYDPEPILCPCF MPAASWSQKRSFVYVWKTWGEGLPSQPIIHTCLLQARLMKEESPVVSWRLEPEDGTALCFIFVYFFLPDHLSFGRPFHLNFCDFLAAPYLGQMINLRR LILISHTHASSYISPEKEEOOAPATEEOEAASSSSTLVEVTLGEVPAAESOAWPFTCLPLGVLMKGQHLHLETFKAVLDGLSTEAEQPFIPVEVLVDLF ${\tt AQDLAGQSLLKDEALAIAALELLPRELFPPLFMEPATQRQDPAAAQEGEDEGASAGQGPKPEAPEAAQPMTKKRKVDGLSTEAEQPFIPVEVLGRCPC}$ GARRPDSRLLQLHITMPFSSPMEAEPGAVLKDFTVSGNLLFIRLTAADHRQLQLSEDIHGTLHLERLAYLHARLRELLCELGRPSDSQEQGHPQTGCE $\tt CEDGPDGQEMDPPMPEEFVIGLRVWQWEVISCKLIKRATTRQPAADADGPGGPGIPDGPGGNAGGPGEAGATGGRPTGHSYVLVTCLGLSYDGLLGDN$ QIMPKTGFLLLKYRAREPVTKAEMLGSVVGNWQYFFPTGILWLLMNNCFLNLSPRKPAAEFQAALSRKVAELVHFLLLKYRAREPVTKAVPDSDPARY EFLWGPRALAETSYVKVLEYVGCCRCGARGPESRLLEFYLAMPFATPMEAEATCLGLSYDGLLGDNQIMPKAGLLIIVLAIGNAGGPGEAGATGGRGP RGAGAARASGPRG

Artificial DNA:

ATAGGGCTAGCCTCTACTCCTTCCCTGAGCCTGAGGCTGCCCAACCCATGACCAAAAAGAGAAAAGGTCGACGGACAGATTATGCCTAAGGCTGGCCTC $\tt CTGATTATCGTCCTGGCTATCATTGCCAGAGAGGGGAGACTGTGCCCCTGAGGAAAAGATTTGGGAACTGCAAGTGCTCGACCTCAGGAAAAACTCCCA$ GAGGTCCCCGGAGCCCAAGGCCAACAGGGACCCAGAGGCAGACAGTCCCCCTCCGTGTCCCAGCTCAGCGTCCTGTCCCTGTCCCGCGTCATGCTCAC $\tt CGTCGTGTCCACCTTTTACGATCCCGAACCCATTCTGTGTCCCTGTTTCATGCCCAATGCCGCTATCGAACTGATGGAGGTCGACCCTATCGGACACC$ $\tt CCCGAACAGTTTAGCGATGAGGTCGAGCCTGCCACACCCGAAGAGGGGAGAGGCTGGCGGATTCTTTCCCTGGCTGAAAGTGTATTACTATAGGTTTTGT$ GATTGGCCTCAGGGTCTGGCAATGGGAAGTGATTAGCTGTGCCGCTATGGAAAGGAGAAGGCTCTGGGGAAGCATTCAGTCCAGGTATATCTCCATGT ${\tt CCGTGTGGACCTCCCCAGAAGGCTCGTGGAAGCCGCTCTGATGGAGACACACCTCAGCTCCAAGAGATACACAGAGGAAGCCGGAGGCTTTTTCCCT}$ TGGCTCAAGGTCTACTATTACAGAGCCGCTATGTCCCTGGAACAGAGAAGCCTCCACTGTAAGCCTGAGGAAGCCCTCGAGGCTCAGCAAGAGGCTCT GGGACTGGTCTGCGTCCAGGCTGCCACAAGCTCCAGCTCCCCCTCGTGCTCGGCACACTGGAAGAGGTCCCCACAGCCGGAAGCACAGACCCTCCCC AAAGCCCTGCCCTCGAGCTCCTGCCTAGGGAACTGTTTCCCCCTCTGTTTATGGCTGCCTTTGACGGAAGGCATAGCCAAACCCTCAAGGCTATGGTC GAGCTCAGCGTCCTGGAAGTGTTTGAGGGAAGGGAAGACTCCATCCTCGGCGATCCCAAAAAGCTCCTGACACAGCATTTCGTCCAGGAAGAGTCCCT GCAACTGGTCTTCGGAATCGATGTGAAAGAGGCTGACCCTACCGGACACTCCTACGTCCTGGTCACCTGTCTGGGACTGTCCCCCGATCCCCTCAGT GGCACAGGCGGAAGCACAGGCGATGCCGATGGCCCTGGCGGACCCGGAATCCCTGACGGACCCGGACAGTGTTTCCTCCCCCGTCTTCCTCGCCCAACC CCCTAGCGGACAGAGAGGGCTGCCACCTGGGGCGAAGGCCTCCCCCCCGGCCTATCATTCACACATGCGTCTACTTTTTCCTCCCCGATCACCTCA GCTTTGGC&G&CCCTTTAGCACAAGCTGTATCCTCG>CCCTGTTTAGGGCTGTGATTACCAAAAAGGTCGCCGATCTGGTCGGCTTTCTGCTCCTG AAATACAGAGCCGCTATGCAAGCCGAAGGCAGAGGCACAGGCGGAAGCACAGGCGGATGCCGATGGCCTGGCGGACCCGGAATCCCTGACGGACCCGG AGACGGACCCGATGGCCAAGAGATGGACCCTCCCAATCCCGAAGAGGTCAAGACACCCGAAGAGGAAATGAGAAGCCATTACGTCGCCCAAATCTCCA ACACTGCAAGACCTCGTGTTTGACGAATGCGGAATCACAGACGATCAGCTCCTGGCTCTCCTCCCTGTCCCTGGGAGACCCTAAGAAACTGCT GCCTCGTGTGTGTGCAAGCCGCTACCTCCAGCTCCAGCCCTCTGGTCCTGGGAACCCTCGAGTTTTACCTCGCCATGCCCTTTGCCACACCCATGGAG GCTGAGCTCGCCAGAAGGTCCCTGGCTCAGGATGCCCCTCCCCTCCCCGTCGAGGAAGCCCCTAGGGGAGTGAGAATGGCTGCCAGACTGCAAGGGCGC TGCCTGGAGACTGGAACCCGAAGACGGAACCGCTCTGTGTTTCATTTTCGCTGCCGAGCAATTCTCCGACGAAGTGGAACCCGCTACCCCTGAGGAAG GCGAACCCGCTACCCAAAGGCAAGACCCTGCCGCTGCCCAAGAGGGAACCATGAACTATCCCCTCTGGTCCCAGTCCTACGAAGACTCCAGCAATCAG CTCATGTGGATCACAGCCGCTATGCCTCTGGAACAGAGAAGCCAACACTGTAAGCCTGAGGAAGGCCTCGAGGCTAGGGGAGAGGCTCTGGGACTGGT CGGCGCTGACGCTGACGGACCCGGAGGCCCTGGCATTCCCGATGGCCCTGGCGGAAACGCTGGCGGACCCGGAGAGGCTGGCGCTACCGGAGGCAGAT ${\tt ACGAATTCCTCTGGGGACCCAGAGCCCTCGTGGAAACCTCCTACGTCAAGGTCCTGCATCACATGGTGAAAATCTCCGGCGGACCCCATATCACAAAC$ TGTAGGCTCAGCGAAGGCGATGTGATGCACCTCAGCCAAAGCCCTAGCGTCAGCCAACTGTCCGTGCTCAGCCTCAGCGGAAACTATCTGGAATACAG ACAGGTCCCGGAAGCGATCCCGCTTGCTATGAGTTTCTGTGGGGCCCTAGGGCTCTGGTCGAGACAAGCTATGTGATTTTCTCCAAGGCTAGGTCCCA

Figure 27 (Cont)

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GGGAAGGCGATTGCGCTCCCGAAGAGAAAATCTGGGAGGAACTGTCCGTGCTCGAGGTCTTCGAAGGCAGAGAGGATAGCATTGACCAACTGCTCAGG ${\tt CATGTGATGAACCCTCTGGAAACCCTCAGCATTACCAATTGCAGACTGTCCGAGGGAGACGTCATGCATCTGTCCAGGGCTCTGGCTGAGACAAGCTA}\\$ $\tt CCCTCGAGTCCTACGAAGACATTCACGGAACCCTCCACCTCGAGAGACTGGCTTACCTCGCCGCTATGCTCATGGCTCAGGAAGCCCTCGCCTTTCTG$ AAGCCTCCAGCTCGTGTTTGGCATTGACGTCAAGGAAGCCGATACCCTCGTGGAAGTGACACTGGGAGAGGTCCCCGCTGCCGAAAGCCCTGACCCTC AATCCCTGTCCCCATTGCGGAGACAGAGTGATGCTGACAGACGTCAGCCCTGAGCCTCTGCAAGCCCTCCTGGAAAGGGCTAGCGCTACCCTCCAGGA ${\tt TCTGGTCTTCGATGAGTGAGGATGAGGGAGCCTCCGCCGGACAGGGGACCCAAACCCGAAGCCGATAGCCAAGAGCAAGGCCATCCCCAAACCGGAT}$ GGAGCCGCTATGTCCTGGAGAGGCAGAAGCACATACAGACCCAGAACCCAGAAGGTATGTGGAACCCCCTGAGATGATCGGACCCATGAGGCCTTACAT AGCATAGCGCTTACGGAGAGCCTAGGAAACTGCTCACCCAAGACCTCGTGCAAGAGAAATACCTCGAGTATAGGCAACAGTGTTTCCTCCCCGTCTTC $\tt CTCGCCCAAGCCCCTAGCGGACAGAGAAGGGCTGCCGTGAAAGTGCTCCACCATATGGTCAAGATTAGCGGAGGCCCTCACATTAGCTATCCCCCTCT$ ${\tt GCATGAGTGGGTGCTCAGGGAAGGCGAACAGCTCCACATTACCATGCCCTTTAGCTCCCCCATGGAGGGCTGAGCTCGTGAGAAGGATTCTGTCCAGGG$ $\tt CTCCTTCCTCATCATTGTGCTCGTGATGATCGCTATGGAAGGCGGACACGCTCCCGAAGAGGGAAATCTGGGAGGAACTGTCCGTGATGGAGGTCGAGG$ $\tt CTCTGGCTAGGAGAGCCTCGCCCAAGACGCTCCCCCTCTGCCTGTGCCTGGCGTCCTGCTCAAGGAATTCACAGTGTCCGGCAATATCCTCGCCGCT$ ${\tt TCCTGCCTAGCCTCAGCCATTGCTCCCAGCTCACCACACTGTCCTTCTATGGCAATAGCATTGTGAAAACCCCTGAGGAAGAGATGAGGTCCCACTAT$ ${\tt AAAAGCTCAAGATTTTCGCTATGCCTATGCCAGAGACATTGCCAGAGAGCCTGTGACAAAGGCTGAGATGCTGGAAAGCGTCATCAAAAACTATAAGCAT$ $\tt TGCTTTCCCGAAATCTTTGGCAAAGCCTCCCTGGTCAGGAGAATCCTCAGCAGAGACGCTGCCCCTCTGCCTAGGCCTGGCGCTGTGCTCAAGGATTT$ $\tt ATCTGATTGGCCTCATGGTCTGGCCTAACCCTTGCCCTCACTGTGGCGATAGGACATTCTATGACCCTGAGCCTATCCTCTGCCCTTGCTTT$ $\tt ATGCCTGCCGCTAGCTGGAGCCAAAAGAGAAGCTTTGTGTATGTGTGGAAGACATGGGGAGAGGGACTGCCTAGCCAACCCATTATCCATACCTGTCT$ $\tt CTCCTGCTCAGCCATATCCATGCCTCCAGCTATATCTCCCCCGAAAAGGAAGAGCAACAGGCTCCCGCTACCGAAGAGCAAGAGCTCCCAGCTCCAGCTCCCAGCTCAGCTCAGCTCCAGCTCCAGCTCAG$ A GCATCTGCATCTGGAAACCTTTAAGGCTGTGCTCGACGGACTGTCCACCGAAGCCGAACCAGCCTTTCATTCCCGTCGAGGTCCTGGTCGACCTCTTC ${\tt TACCGTCAGCGGAAACCTCCTGTTTATCAGACTGACAGCCGCTGACCATAGGCAACTGCAACTGTCCGAGGATATCCATGGCACACTGCATCTGGAAA}$ TGTGAGGATGGCCCTGACGGACAGGAAATGGATCCCCCTAACCCTGAGGAATTCGTCATCGGACTGAGAGTGTGGCAGTGGGAGGTCATCTCCTGCAA GAATTCCTCTGGGGACCCAGAGCCCTCGCCGAAACCTCCTACGTCAAGGTCCTGGAATACGTCGGCTGTTGCAGATGCGGAGCCAGAGGCCCTGAGTC AGAGGCGCTGGCGCCCAGAGCCTCCGGCCCTAGGGGA

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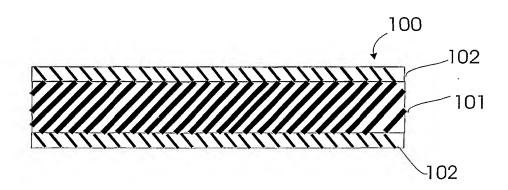


FIGURE 28

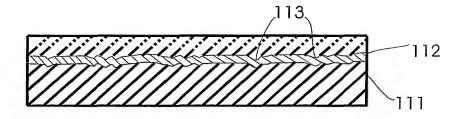


FIGURE 29

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Cassettes for construction of a full-length HIV Savine

Cassette Al

ggatccaccATGACAGGCCCTTGCACAAACGTCAGCACCGTGCAATGCACACACGGAATCAGACCCGTCGTGTCCA CCCAACTGCTCCTGAATGGCTCCCTGAGAAGCCTCTACAATACCGTCGCCACACTGTGGTGCGTCCACCAAAGGAT TGACGTCAGGGACAAAGGAAGCCCTCGACAAAATCGAACTCGGCGATGGCGGAGGCGCTGAAAGGCAAGGCACC TCCAGCTCCTTCAACTTTCCACAAATCACACTGTGGCAAAGGCCTCTGGTCACCGAACCCTTCAGAAAAAAGAATC $\tt CCGATATGGTGATTTACCAGTACATGGACGATCTGTATGTGGGAAGCGATCTGGAAATCGGACAGCATTTTACCAC$ ACCCGATAAGAACACCAAAAGGAACCACCATTCCTCTGGATGGGATACGAACTGCATCCCGATAGGTGGACCGTC CAGCCTCTTAATTTCCCTCAGATTACCCTCTGGCAGCGTCCCCTCGTGACAATCAAAATCGGCGGACAGCTCATAG AGGCTCTGCTCGACACAGGCTCCTATGGCAGAAAGAAACGTAGGCAACGTAGACGCGCTCCTCAGAGCAGCAAGGA TCACCAATACCCTATCTCTGAGCAACCCCTCTCCTTCTTTAGGGAAAACCTGGCTTTCCAGCAAGGTAAAGCCAGA GAGTTTTCCAGCGAACAGACAAGAGCCAATAGCTCCGCCTCCAGGAAGAGCCCCCAAATCTCCGGCGAAAGCTCCG TCATTCTGGGATCTGGCACCAAAAACGCCGCTACTAGAAGAATCGAAGTGAAAGATACCAAAGAGGCTTTGGATAA GATTGAGGAGGTGCAAAAGAAAAGCGAGCAAAAGACACAACAGGCTGCCGCTAAAGCCGGATACGTCACCGATAGG GGAAGGCAAAAGATTATCTCCCTGACAGAGACAACCAATCAGAAAACCGAACTGCATGCCATTCAAGAAGCCACTA CCACACTGTTTTGCGCCAGCGATGCCAAAGCCTATGAGACAGGGTCCACAATGTGTGGGCCACACACGCTTGCGT $\tt CCCCGCTGACGATACAGTGCTGGAGGAGATGAACCTCCCCGGAAAATGGAAGCCTAAGATGATTGGCGGAATCGGC$ GGATTCATTAAGGTGAGAAAAATCGGACCCGAAAACCCTTACAATACCCCAATCTTCGCTATCAAGAAAAAGGACT $\tt CTCCGAAGGCTCCAGGCAAACCAGAAGAATAGGAGAAGGAGGAGGGGAGGCGAACGGGGTAGGGATAGGTCCGTG$ AGACTGGTCAACGGATTCTTAGCCCTCGCCTGGGACGATCTGAGAAACCTCTGCCTCTTCGAAAACCTCTGGGTCA CCGTCTACTATGGCGTCCCCGTCTGGAGAGAGGCTGCCACAACCCTCTTCTGTGCCTCCGACGCTAAGGCTTACGC TGCCATGGCTGGCAGAAGCGGCGCACAGACGAAGAGCTCCTGAGGGCTATCAGAATCATTAACATTCTGTATCAG TCCAACCCTTACCCTTCCGCTAGTATGAGAATCAGAACCTGGAACAGCCTGGTCAAGCATCACATGCACATCTCCA AGAAAGCCAAAGGCTGGTTCTATAGGCATCACTTTGAGGAGTCCGAGCTCGTGAATCAGATTATCGAAAAGCTCAT CAAAAAGGAAAAGGTCTACCTATCATGGGTACCAGCCCACAAGGGAATCGGACAAACCAAAGAGCTCCAGAAACAG ATTATCAAAATCCAAAACTTTAGGGTCTACTATAGGGATAGCAGAGACCCTATCTGGAAGGGACCCAAAAGCTTTG TCTGAAACCCGAACCCACAGCCCCTCCCGCTGAGAATTTCAGATTCGGTGAGGAAACTACACCCTCCCAAAAGCAA GAGCAAAAGGATAAGGAGCAATACGATCAGATTCTTATTGAGATTTGCGGCAAGAAAGCTATTGGTACGGTGCTCG TGGGACCTACCCCTGTGAATATCATTGGCAGAATTTACGAAACCTATGGCGATACCTGGGAGGGCGTCGAGGCTCT GATCAGAATCCTCCAGCAACTGATGTTTATCCATTTCAGAATCGGATGTTTTCATTGCCAAGTGTGTTTTCTCACC TGGACCCCAAGCTGGAGCCTTGGAAACACCCTGGCTCCCAGCCTAAGACAGCCTGTTACAAATGCTATTGCAAAAA GTGCCCTAGCGAAGAGACCCCCTAGCCAGAAACAGGAACAGAAAGACAAAGAACTCTACCCCCCTTTAGCCAGC CTCAAGTCCCTGTTTGGCAATGACAATTTCAATATGTGGAAGAATGACATGGTGGAACAGATGCAAGAAGACATTA TCTTACTATGGGACCAAAGCCTCAAGCCTTGCGTCAAGCTCGACGTCGGCGATGCCTATTTCTCCGTGCCTCTGGA GGCCAAGTGAATTGCTCACCAGGCATTTGGCAACTGGATTGCACACCCTGGAGGGAAAGATTATCCCTAAGGTCA TAGCATGGATGACCTCTACGTCGGCTCCGACCTGG

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AGATTGGCCAACATAGGACCAAAATCGAAGAGCTCAGGGAACACCTCCTGAAATGGGGACTCACCGAAACCACAA CAGACAATGGCAGGACAAAGATTGAGGAACTGAGACCGCATCTGCTCAAATGGGGCTTCACAACCCCTGACAAAAA AAGAGACGCAGAGAAAATCACACAATGAATGGCCATACTGCCACAGAGTCCCAGAATCAGCAAGACAGAAACGAAA AGGAACTGCTGGACCAAATGGGCAAGCCTCTGGAATTGGTTTAACATTACCGACACCGGAAATAGCTCCAA AGTGTCCCAGAATTACCCTATCGTCCAGAATGTCCAAGGCCAAATGGTCCACCAACCCCTCTCCCCCAGACTCATC GGACTGAGAATCGTTTTCGCTGTGCTCAGCATTATCAATAGGGTCAGGCAAGGCTATAGCCCTCTGTCCTAAA $\tt CCCTCCCCTCATCCATCTGCAATACTTTGACTGTTTCGCTGACTCCACCATTAGGAGAGCCATCTTGGGACACAT$ AGTGAGAAGGAGATGCGAATACGCTGTGGGACTCGGAGCCATGTTCCTTGGCTTCTGGGTGCCGCTGGCTCCACC ATGGGCGCTGCCTCCATGACACTGACAGTGCAAGCCTATGACCCTAGCAAAGACCTCATTGCTGAGATTCAGAAAC AGGGCCAGGGTCAGTGGACATTTCAGATTTTCCAAGAGCCTTTCAAAAACGGAACCGTCCTGGTCGGCCCTACACC CGTCAACATCATCGGAAGGAACATGCTGACACAGCTTGGCCGCACTCTCAACTTTCCCATTAGCAAAGGCAGCCCT GCTATCTTTCAGTCCAGCATGCCACAGATTCTGGAGCCTTTTAGGATAAAAAACCCTGAGATGGTCATCTATCAGT GGGCGAAAACAATTGCCCCCTGTTTAGGAAATACACAGCCTTTACCATTCCCTCCATCAATAACGAAACCCCTGGC ATTAGGTATCAGTATAACGTCCTGCCTCAGGGATGGGGAAGCACAATGGGAGCCGCCAGCATGACCCTCACCGTCC AGGCTAGGCTACTGCTCAGCGGAATCGTCCAGCAACAGAGCAATCTGCTGGAGGAGAATAGGGAAATCCTCAGAGA GCCTGTGCATGCGTCTACTACGATCCCTCCAAGGATCTGGTCGCTGAAATCCAAAAGCAAGGCAGAGAGGAACTG TCCACCATGGTGGATATGGGAAACTACGACCTCGGAGTGGACAATAACCTCGCCGCTATTAGAATCCTGCAACAGC TCATGTTCATTCACTTTAGGATTGGCTGCCAGCACTCCAGGATTGGCATCATCCGTCAGAGAGGGCCAGAGCTCC CAGGAAAAAGGGATGCTGGAAGTGTGGCAGAGAGGGGACACCAGATGAAGGATTGCACTGAGAGACAGGCTAACTTT ATGGCGTCAGCATTGAGTGGAGGATAAGGGAAAGGGCTGAGGATAGCGGCAACGAAAGCGAAGGCGACACAGAAGA GCTCAGCACATTGGTGGACATGGGCAATTACGATCTGTCTAGCCCTGCCCCCAGGGGACCCGATAGGCTGGAGAGA ATCGAAGAGGAGGCGGAGAGCAAGGCAGAGGCAGAAGCGTCAGGCTCGTGAATGGCAGAGAGGTCGAGGAAGTCA GTGGCCAGCTTCTCTCCGAGCAAACAGGGGCTAACTCCTCTACAAGCAGAAAGCTGGGAGACGGAGGCGGAGCCG ACAGACAGGGAACAAGCTCCAGCTGTTTCAATTGCGGCAAAGAGGGGACACATTGCCAAAAACTGTAGGGCCCCTCG CAAGAAAGGTTGTTGGAAATGCGGAAAGGAAGGCCATCAAATGAAAGACTGTACCGAAAGGCAAGCCAATTTCCTC GGCAAAATCTGGCCCTCCAACAAAGGCAGACCCGGAAACTTTCTCCAAAGCAAATGGCTCTGGTATATCAAAATCT TTATCATGATCGTCGGTGGACTGATTGGCCTCAGGATTATCTTTGCCGTCCTGTCCATCGTTAACGGAGCCGTGAG CCGAGACCTCGATAAACATGGCGCTATTACAAGCTCCAATACCGCTGCCAATAACGCTGACTGTGTCTGGCTGAAG GCTGCTGCCATGACACCCCTGGAGATCATCGCTATCGTCGCCTTTATCGTCGCCCTCATCATAGCCATTGTGGTCT GGACAATCGTCTACATTGAGTATGTCGACtgaagatctgaattc

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A2 fragment

ggatccaccATGACAGGCCCTTGCACAAACGTCAGCTCCGTGCAATGCACACACGGAATCAAACCCGTCGTGTCCA $\tt CCCAACTGCTCCTGAATGGCTCCCTGAAAAGCCTCTACAATACCGTCGCCACACTGTGGTGTCCACCAAAGGAT$ TGAGGTCAAGGACACAAAGGAAGCCCTCGACAAAATCGAACTCGGCGATGGCGGAGGCGCTGAAAGGCAAGGCACC TCCAGCTCCATCAACTTTCCACAAATCACACTGTGGCAAAGGCCTCTGGTCACCGAACCCTTCAGAAAAGAGAATC ACCCGATAAGAAACACCAAAAGGAACCACCATTCCTCTGGATGGGATACGAACTGCATCCCGATAGGTGGACCGTC CAGCCTTTAATTTCCCTCAGATTACCCTCTGGCAGCGTCCCTCGTGACAATCAAAATCGGCGGACAGCTCATAG AGGCTCTGCTCGACACAGGCTCCTATGGCAGAAAGAAACGTAGGCAACGTAGACGCGCTCCTCAGAGCAGAAAGGA TCACCAATACCCTATCTCTGAGCAACCCCTCTCCTTCTTTAGGGAAAACCTGGCTTTCCAGCAAGGTAAAGCCAGA GAGTTTTCCAGCGAACAGACAGGAGCCAATAGCTCCGCCTCCAGGAAGAGCCCCCAAATCTCCGGCGAAAGCTCCG TCATTCTGGGATCTGGCACCAAAAACGCCGCTACTAGAAGAATCGATGTGAGAGATACCAAAGAGGCTCTGGATAA GATTGAGGAGGAGCAAAACAAAAGCAAGCAAAAGACACAGGCTGCCGCTAAAGCCGGATACGTCACCGATAGG GGAAGGCAAAAGATTATCTCCCTGACAGAGACAACCAATCAGAAAACCGAACTGCATGCCATTCAAGAAGCCGATA $\tt CCACACTGTTTTGCGCCAGCGATGCCAAAGCCTATGACACAGGGTCCACAATGTGTGGGCCACACACGCTTGCGT$ CCCCGCTGACGATACAGTGCTGGAGGAGATGAACCTCCCCGGAAAATGGAAGCCTAAGATGATTGGCGGAATCGGC $\tt GGATTCATTAAGGTGAGAAAGATCGGACCCGAAAACCCTTACAATACCCCAATCTTCGCTATCAAGAAAAAGAACT$ CCACCAAATGGAGAAAGCTCGTGGATTTCAGAATTAGGATTATCAAAATCCTCTACCAAAGCAATCCCTATCCTAG CTCCGAAGGCACCAGGCAAACCAGAAAGAATAGGAGAAGGGGATGGGGAGGCGAACAGGGTAGGGATAGGTCCGTG AGACTGGTCAACGGATTCTTAGCCCTCGGCACGATCTGAGAAGCCTCTGCCTCTTCGACAACCTCTGGGTCA TGCCATGGCTGGCAGCAGCAGCACAGACGAAGAGCTCCTGAAGGCTGTCAGAATCATTAAGATTCTGTATCAG TCCAACCCTTACCCTTCCGCTAGTATGAAAATCAGAACCTGGAAGAGCCTGGTCAAGCATCACATGTACATCTCCA AGAAAGCCAATGGCTGGTTCTATAGGCATCACTTTGAGGAGTCCGAGGTCGTGAATCAGATTATCGAAAAGCTTAT CAAAAAGGAAAAGGTCTACCTATCATGGGTACCAGCCCACAAGGGGAATCGGACGAACCAAAGAGCTCCAGAAACAG ATTATCAAAATCCAAAACTTTAGGGTCTACTATAGGGATAGCAGAGACCCTATCTGGAAGGGACCCAAAAGCCTTG TCTGAGACCCGAACCCACAGCCCCTCCCGCTGAGAATTTCGGATTCGGTGAGGAAACTACACCCTCCCAAAAGCAA GAGCCAAAGGATAAGGAGCAATACGATCAGATTATTATTGAGATTTGCGGCAAGAAAGCTATTGGTACAGTGCTCG TGGGACCTACCCCTGTGAATATCATTGGCAGAATTTACGAAACCTATGGCGATACCTGGGAGGGCGTCGAGGCTCT GATCAGAATCCTCCAGCAACTGATGTTTATCCATTTCAGAATCGGATGTTTTCATTGCCAAGTGTGTTTTCTCACC TGGACCCCAACCTGGAGCCTTGGAAACACCCTGGCTCCCAGCCTAAGACAGCCTGTAACAAATGCTATTGCAAAAA CTCAAGTCCCTGTTTGGCAATGACAATTTCAATATGTGGAAGAATAACATGGTGGAACAGATGCAAGAAGACATTA GGCCAAGTGAATTGCTCACCAGGCATTTGGCAACTGGATTGCACACCCTGGAGGGAAAGATTATCCCTAAGGTCA TAGCATGGATGACCTCTACGTCGGCTCCGACCTGGAGATTGGCCAACATAGGACCAAAATCGAAGAGCTCAGGGCA

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CACCTCCTGAGATGGGGACTCACCGACACCACAAACCAAAAGACTGAGCTCCACGCTATCCATCTGGCTCTGCAAG ACTCCGGCTTAGAGGTCAACATTGTGACAGACATTCCCGCTGAGACTGGTCAAGAGACCACCTATTTCATTCTGAA ${\tt ACTGGCTGGCAGATGGCCTGTGAGAATCATTCACACAGACAATGGCAGGACAAAGATTGAGGAACTGAGACCGCAT}$ CTGCTCAAATGGGGCTTCACAACCCCTGACAAAAAGCGTCAGAAAGAGCCTCCCTTTCTGTCTAGTGTCAAGAAAC CACAGAGTCCCAGAATCAGCAAGACAGAAACGAAAAGGAACTGCTGGAGCTCGACAAATGGGCAAGCCTCTGGAAT TGGTTTAACATTACCGACACCGGAAGTAGCTCCCAAGTGTCCCAGAATTACCCTATCGTCCAGAATCTCCAAGGCC AAATGGTCCACCAACCCATCTCCCCCAGACTCGTCGGACTGAGAATCATTTTCGCTGTGCTCAGCATTATCAATAG GACTCCACCATTAGGAGAGCCATCCTTGGACACAGAGTGAGCAGGAGATGCGAATACGCTGTGGGAATCGGAGCCA $\tt CCCTAGCAAAGACCTCATTGCTGAGATTCAGAAACAGGGTCAGGATCAGTGGACATATCAGATTTTCCAAGAGCCT$ ${\tt GCACCCTCAACTTTCCCATTAGCAAAGGCAGCCCTGCTATCTTTCAGTCCAGCATGACACAGATTCTGGAGCCTTT}$ TAGGAAACAAAACCCTGACATGGTCATCTATCAGTATCCTAGCCCTCTGACATTCGGATGGTGTTTCAAACTGGTC $\verb|CCCGTGGACCCCAGCGAAGTGGAAGAGACCAACAAGGGCGAAAACAATTGCCTCCTGTTTAGGAAATACACAGCCT|\\$ TTACCATTCCCTCCACCAATAACGAAACCCCTGGCATTAGGTATCAGTATAACGTCCTGCCTCAGGGATGGGGAAG CACAATGGGAGCCGCCAGCATGACCCTCACCGTCCAGGCTAGGCAACTGCTCAGCGGAATCGTCCAGCAACAGAAC AATCTGCTGGAGGAGAATAGGGAAATCCTCAAAGAGCCTGTGCATGGCGTCTACTACGATCCCTCCAAGGATCTGA TCGCTGAAATCCAAAAGCAAGGCACAGAGGAACTGTCCGCCTTGGTGGATATGGGAAACTACCACCTCGGAGTGGA ATTGGCATCATCCGTCAGAGAAGGGCCAGAGCTCCCAGGAAAAAGGGATGCTGGAAGTGTGGCAAAGAGGGACACC AGATGAAGGATTGCACTGAGAGACAGGCTAACTTTCTGGGAAAGGATGCCAGACTGGTTATCAAAACCTATTGGGG ACTGCATACCGGTGAGAGAGACTGGCACCTCGGCCATGGCGTCAGCATTGAGTGGAGGACAAGGGAAAGGGCTGAG GATAGCGGCAACGAAAGCGAAGGCGACAGAGAGAGAGCTCAGCACAATGGTGGACATGGGCAATTACGATCTGTCTA GCCCTGCCCCCAGGGGACCCGATAGGCTGGAGAGAATCGAAGAGGAGGAGGCGGAGAGACAGAAGACAGAAGCGT CAGGCTCGTGAATGGCAGTGAGGGCGAGGAAGTCAATAAGGGAGAGAATAACTGTCTGCTCCACCCTATGAGTCAA CATGGCATGGAAGACGAAGACAGAGGTCAATAGCGATATCAAAGTGGTCCCCAGAAGGAAAGCCAAAATCATTA GGGATTACGGAAAGCAAATGGCTGACGATGACTGTGTGGCCGGCTTCTCTTCCGAGCAAACAAGGGCTAACTCCCC ${\tt GAGGGACACATTGCCAAAAGCTGTAGGGCCCTCGCAAGAAAGGTTGTTGGAAATGCGGAAGGGAAGGCCATCAAA}$ TGAAAGACTGTACCGAAAGGCAAGCCAATTTCCTCGGCAAAATCTGGCCCTCCAAAAAAGGCAGACCCGGAAACTT TCTCCAAAGCAAATGGCTCTGGTATATCAAAATCTTTATCATGATCGTCGGTGGACTGATTGGCCTCAGGATTATC TTTGCCGTCCTGTCCATCATTAACGGGGCCGTGAGCCGAGACCTCGATAAACATGGCGCTATTACAAGCTCCAATA CCGCTGCCAATAACCCTGACTGTCTGGCTGGAGGCTGCTGCCATGACACCCCTGGAGATCATCGCTATCGTCGC CCTTATCGTCGCCCTCATCATAGCCATTGTGGTCTGGACAATCGTCTACATTGAGTATGTCGACtgaagatctgaa ttc

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B1 fragment

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TCCCTGAAACCCTGTGTGAAACTGACACCCCTCTGCGTCACCCTCAACTGTACCAATGCCAATCTGATGAAGAGAT ACTCCACCCAAGTGGACCCGATCTGGCTGACCAACTGATTCACCTCCACTATTTCGATTGCTTTGCCGATAGCGC AATCCATCCCATCGGCCAACACGGAATGGAGGATGAGGGATAGGGAAGTGCTGAAATGGAAATTCGATAGCCATCTG ${\tt TGAAACACTGGCCCTCACCGAAGAGAAAATCAAAGCCATTTGGCCTAGCAACAAGGGAAGGCCTGGCAATTTCCCC}$ ${\tt GCAGTCCAGGCCTGAGCCTACCGCACCCCAGCCGAGAGCTTTAGATTCGGCATTAGCAAAAAGGCTAAGGGATGG}$ $\tt TTTTACAGACACCATTACGATAGCCGACACCCTAAGGTCAGCTCCGAGGTCCACATTCCCCTCGGCATGATGACCG$ CATTCCTCCCATTGTGGCCAAAGAGATTGTGGCAAACTGTGACAAATGCCAGCTCAAGAGTGAGGCTATTCACGGA GGCAAATCCACTCCATCTCCGAGAGGATTCTGGGACAGATGAGGGAACCCAGAGGCTCCGACATTGCCGGTACTAC AAGCACACTGCAAGAGCAAATCGCATGGATGACAAGCAATCCCCCTAGCATTCAACAAGAGTTTGGCATTCCCTAT AACCCTCAGTCCCAGGGCGTCGTGGAAAGCATGAACAAAGAGCTAAAGAAAATCATTGGCAGACAGGAGATCCTCG ATCTCTGGGTCTACCATACCCAAGGCTATTTCCCTGACTGGCAGAATTACACACCCGGACCCGGAGTCAGATACCC TAGCAGAGAAAGACAGAGACAGATTCATTCATTAACGAATGGATTCTCAGCAACTGCCTCGGCAGATCCGCTGAG $\verb|CCTGTGCCTCTGCAACTGTATAAGACACTGAGAGCCGAACAGGCTACCCAAGAGGTCAAGAATTGGATGACCGAGA|\\$ CACTGCTCGTGCAAAACGCTAACCCTGACTGTGAGAGAGTGTATCTGGCTTGGGTCCCCGCTCATAAAGGCATTGG CGGAAACGAACAGGTGGACAAACTGGTCAGCGCTGGCATTAGGAAAACAGACCCTAACCCTCAGGAAATCCATCTG TGAAATGCAATAACAAAAGGTTCAACGGAACTGGACCCAGTAAGAATGTGTCCACCGTCCAGTGTACCCATGGCCT AGAGCTCAAGAATAGCGCTATCTCCCTGCTCAACGCTACCGCTATCGCTGTGGCTGGGTGGACCGATAGGGTTATC GAAGTGGTTCAGTCCCGGCATCCCAAAGTGTCCAGCGAAGTGCATATCCCTCTGGGAGACGCTAGGCTCATCATTA GGACATACTGGGGCCTCCACACAGGCGCTGCTATGGGCGGTAAATGGTCCAAGTGCTCCCTCGTCGGATGGCCCGC AGTGAGAGAGAATCAGACAGACACCCCCTGCCGCTGAGGGAGTGCTCAAGACCGGCAAGTACTCTAGGAAGAGG GGTGCCCATACCAATGACGTCAAGCAACTGACAGAGGCTGTGCAAAAGATTGCCACAGAGTCTAGCTGGGAGGGTC AGCCATTGAGCTGCCTGAGAAAGCTGGACCGTCAACGATATCCAAAAGCTCGTGGGAAAGCTCAACTGGGCA ${\tt TGCAAGCCAGAGTGCTCGCCATTGAGAGATACCTCGCCCTCCAGGATAGCGGATTGGAAGTGAATATCGTCACCGA}$ TAGCCAATACGCTCTAGGCATCATTCAGGCTCAGCCTGACAAAAGCGAAAGGGAAATCTCCAACTATACCAATCAG ATTTACAAGATCCTCACCGAATCTCAAAATCAACAGGATAGGAATGAGAAAGACCTCCTGGCTCCCACAAAGGCTA ${f AGAGAAGGGTCGTGCAAAGGGAAAAGCGTGCCGTCGGCATTGGCGCTATGTTTCTCGGATTCCTCGGCGCTGCCAA}$ ACCCAAAATGATCGGAGGCATTGGAGGCTTTATCAAAGTCAGGCAGTATGACCAAATCCTTATCGAAATCTGTGGA AACAAGGCTATCTCCTACCATAGGCTCAGGGATTTCATTCTGATCGTCGCTAGGATTGTGGAACTGCTCGGCCGTA GCTCCCTGAAAGGCCTCCAGAGAGGCACACTGAATGCCTGGGTGAAAGTGATTGAGGAAAAGGGATTCAGTCCCGA AGTGATTCCCATGTTTTCCGCTCTGTCCGAGGGAGCCACACTCGAGtgaagatctgaattc

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B2 fragment

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TCCCTGAAACCCTGTGTGAAACTGACACCCCTCTGCGTCACCCTCAACTGTACCAATGCCAATCTGCTGAAGAGCT ${\tt ACTCCACCCAAGTGGACCCCGATCTGGCTGACCATCTGATTCACCTCCACTATTTCGATTGCTTTTCCGATAGCGC}$ AATCCATCCCATGGGCCTACACGGAATGGAGGATGAGGAAAGGGAAGTGCTGAAATGGAAATTCGATAGCCATCTG GCAGTCCAGGCCTGAGCCTACCGCACCCCAGCCGAGAACTTTAGATTCGGCATTAGCAAAAAGGCTAAGGGATGG $\tt TTTTACAGACACCATTACGAAAGCCAACACCCTAAGGTCAGCTCCGAGGTCCACATTCCCCTCAGCATGATGACCG$ $\tt CTTGCCAAGGCGTCGGCGGACCCAGTCACAAAGCCAGGGTACTGGCAGAGGCTATGTCCCAGGTGAACAACGCTAA$ CATTCCTCCCATTGTGCCCAAAGAGATTGTGGCAAACTGTGACAAATGCCAGCTCAAGGGTGAGGCTATGCACGGA CAGGTGGACTGTAGCCCTTCCGAGGGATCAAGACAGGCTAGGAAGAACAGACGTAGAAGGTGGCGTGAGAGGCCAAA GGCAAATCCGCGCCATCTCCGAGTGGATTCTGGGACAGATAAGGGAACCCAGAGGCTCCGACATTGCCGGTACCAC AAGCACACTGCAAGAGCAAATCGCATGGATGACAAACAATCCCCCTGGCATTAAGCAAGAGTTTGGCATTCCCTAT AACCCTCAGTCCCAGGGCGTCGTGGAAAGCATGAACAAAGAGCTCAAGAAAATCATTGGCAGACAGGAGATCCTCG ATCTCTGGGTCTACAATACCCAAGGCTTTTTCCCTGACTGCAGAATTACACACCCCGGACCCGGAATCAGATACCC TAGCAGAGCAAGACAGAGACAGATTCATGCTATTAGCGAAAGGATTCTCAGCAACTTCCTCGGCAGACCCGCTGAG $\verb|CCTGTGCCTCTGCAACTGTATAAGACACTGAGAGCCGAACAGGCTACCCAAGAGGTCAAGAATTGGATGACCGACA|\\$ CACTGCTCGTGCAAAACGCAAACCCTGACTGTGAGAAAGTGTATCTGGCTTGGGTCCCCGCTCATAAAGGCATTGG CGGAAACGAACAGGTGGACAAACTGGTCAGCGCTGGCATTAGGAAAACAGACCCTAACCCTCAGGAAATCGATCTG TGAAATGCAATAACAAAAAGTTCAACGGAACTGGACCCTGTAAGAATGTGTCCACCGTCCAGTGTACCCATGGCCT AGAGCTCAAGAATAGCGCTGTCTCCCTGCTCAACGCTACCGCTATCGCTGTGGCTGAGTGGACCGATAGGGTTATC GAAGTGGTTCAGTCCCAGCATCCCAAAGTGTCCAGCGAAGTGCATATCCCTCTGGGAGACGCTAGGCTCGTCATTA AGACATACTGGGGCCTCCACACAGGCGCTGCTATGGGCGGTAAATGGTCCAAGTGCTCCCTCGTCGGATGGCCCGC AGTGAGAGAGAGATCAGACAGACACCCCCTGCCGCTGAGGGAGTGCTCAAGACCGGCAAGTACTCCAGGATGAGG TGAAATACTTGTGGAATCTGCTCCTGTACTGGGGCCTGGAACTGAAAAACTCCGCCGTCAGCCTCCTGAATGCCAC AGCCATTGTGCTGCCTGAGAAAGGAGGCTGGACCGTCAACGATATCCAAAAGCTCGTGGGAAAGCTCAACTGGGCA TGCAAGCCAGAGTGCTCGCCATTGAGAGATACCTCGCCCTCCAGGATAGCGGATCGGAAGTGAATATCGTCACCGA TAGCCAATACGCTCTAGGCATCATTCAGGCTCAGCCTGACAAAAGCGAAAGGGAAATCTCCAACTATACCAATCAG ATTTACAAGATCCTCACCGAATCTCAAAATCAACAGGATAGGAATGAGCAAGAACTCCTGGCTCCCACAAAGGCTA AGAGAAGGGTCGTGCAAAGGGAAAAGCGTGCCGTCGGCATTGGCGCTATGTTTTTCGGATTCCTCGGCGCCTGCCAA ACCCAAAATGATCGGAGGCATTGGAGGCTTTATCAAAGTCAGGCAGTATGACCAAATCCTTATCGAAATCTGTGGA CAGAAGGCTATCTCCTACCATAGGCTCAGGGATTTCATTCTGATCGTCGCTAGGATTGTGGAACTGCTCGGCCATA GCTCCCTGAGAGGCCTCCGGAGAGGCACACTGAATGCCTGGGTGAAAGTGGTTGAGGAAAAGGGATTCAATCCCGA AGTGATTCCCATGTTTACCGCTCTGTCCGAGGGAGCCACACTCGAGtqaaqatctqaattc

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C1 fragment

ggatccaccATGCTCGAGAGCAACACCCGCTAATAATGCCGATTGCGCGTGGCTGAAAGCCCAGGAAGAGGAAAG A AGTGGGATTTCCTGTGAGACCCCAAGTGCCTAGAGCTTGGAGGGCTATCCTCAACATTCCCAGGAGGATTAGGCAAGGCTTTGAGAGAGCCCTCCTAGCCGCCGAATGGGACAGGGTTCACCCTGTGCACGCTGGCCCTGTCGCTCCCGGC TCAGCTTGTTTCTGAAAGAGAAAGGCGGACTGGAAGGCCTCATCTATAGCAAGAAAGCTGCTATGGAACAGGCTCC ${\tt CAAGGCCAATGGACCTACCAAATCTTTCAGGAACCCTTTAAGAATCTGAAAACCGGAAAGTATTCCAGAATGAGAA}$ GCGCTCACACAAACTGGATGACAGAAACCCTCCTGGTCCAGAATGCCAATCCCGATTGCAAGTCCATCCTCAGGGC TCTGGGAACCGGAGCCACACTGGAAGAGCCTGAGGTCATCCCTATGTTCTCAGCCCTCAGCGAAGGCGCTACCCCC ${\tt CAAGACCTGAATACGATGCTCAACATCGTCAGCGGACACCAATCCACCCTCCAGGAACAGATTGGCTGGATGACAA}$ ATAACCCTCCCATCCCTGTCGGAGAGATTTTACAAAAGGTGGATTATCCTCGGCCTGACTAGAATCCCCCATCCCGC CAAAAGGAAACCTGGGAGGCTTGGTGGACGGAATACTGGCAGGCTACCTGGATTCCTGAGTGGGAGTTTGTGAATA TTTTACGTGGACGGAGCCGACAGAGAGACAAAGCTCGGCCAAAACGTCCAGGGACAGATGGTGCATCAGGCTA TTAGCCCCAGGACCCTCAACGCTTGGGTCAAGGTCGTCGAAGAGAAAGCCTTTAACGAAACCGAAGTGCATAACGT $\tt CTGGGCTACCCATGCCTGTGTGCGTACCGATCCCCAATCCCCAAGAGATTCTCCTGGAGAATGTGACAGAGCTCAAG$ GATCAGAAACTCCTCGGCATTTGGGGATGCTCCGGCAAAATCATTTGCACAACCACTGTGCCTTGGAACAGCTCCT GGTCCAACCAAGCTGGCCATAACAAAGTGGGAAGCCTCCAGTATCTGGCTCTGACGGCTCTGATTAAGCCTAAGAA AATCAAACCCCCTCTGCCTAGCGTTAAGACAATCATTGTGCATCTGAATGAGTCCGTGGAAATCAATTGCACAAGG CCTAACAATAACACAAGGAAAGCCGCCGCTAGTGAAGTACGGAATAAGTCCAAACAGAAAACCCAGCAAGCTGCCG $\tt CGCTTGTTGGTGGGCCAATATCAAACAGGAGTTTGGAATCCCTTACAATCCCCAAAGCCAAACATTCTATGTGGAT$ GAATCTGGCAGCTCGACTGTACCCATCTGGAAGGCAAAGTCATTCTGGTAGCCGTCCACGTCGCCTCCGGCTACAT ${\tt TGAGGCTGAGGTCGGCAATGAGCAAGTGGATAAGCTCGTGAGTTCCGGAATCAGAAAGGTGCTATTCCTCGACGGA}$ ATCAATAAGGCTCAGGAAGAGCACGAAGTCAGGGAAAGGATTAGGCGAACCGCTCCCGCTGCTGAAGGCGTCGGCG CTGTCTCCCAGGATCTGGATAAGTACGGAGCCCTCACCTCCACAAGCGGAACCCAACAGTCCCAGGGAACTGAAAC TGGCGTCGGCAACCCTCAGATTTTGGGAGAGTCCAGCGTTGTCCTCGGCTCCGGCTCCATCGTCATCTGGGGTAAA ${\tt ACCCCTAAGTTTAAGTTCCCCATTCAGAAAGAGACATGGGAAGCCTGGTGGACGGAGTATTGGCAAGCCGCTGCTT}$ ${\tt ACAGACTGATCAGCTGTAACACAGCGTTATCAAACAGGCTTGCCCTAAGATTACCTTTGACCCTATCCCTATCCA}$ TTACTGTGCCCCTCTAGCTGGATGGGCTATGAGCTCCACCCTGACAGATGGACAGTGCAACCCATCGTGCTCCCC GAAAAGGACTCCTGGACAGTGAATGACATTCAGAAATCAATTCTGAGAGCCCTCGGCCCAGGCGCTTCCCTGGAGG CATTTGGAAAGGCCCTGCCAAACTGCTCTGGAAAGGCGAAGGCGCTGTGGTCATCCAAGACATTAAGATTGGAGGC ${\tt GAATCAAACAGCTCCAGGCTAGGGTCCTGGCTATCGAGAGGTATCTGAAAGATCAACAGTTTCTGGGACTCTGGGG}$ CTGTAGCGGAAAGGCTGCTATGGAAAACAGATGGCAAGTGATGATCGTCTGGCAAGTGGACAGGATGAAGATTAGG

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ACATGGAATAGCCTCGTGAAACACCATATGTATATTATCTGTACCACAACCGTCCCCTGGAACTCCACCTGGAGCA ATAAGTCCTTCGAAGAGATTTGGAATAACATGACCTGGATTCAATGGCTGATTCTCGCTATCGTCGTGTGGACCATTGTGTATATCGAATACAAGAAACTGCTCAGGCAAAGGAGAATCGATAGGCTCATCAAAAGGCTCAACCCTGGCCTC $\tt CCCATTTTCCAAAGCTCCATGACCCAAATCCTCATGATGCAAAGGGGAAAACTTTAAGGGACAGAAAAGGATTATCA$ AGTGCTTCAACTGTGGAAAGGAAGGCCATCTCGCTAGGAATTGCAGACCTCCCCTAGAGAGACTGAACCTGGATTG $\tt CTCCGAGGATAGCGACACCTCCGGCACACAGCCAAAGCCAAGGCACAGAGACAGAAGTGGGACTCGTGGCTGTGCAT$ $\tt GTGGCCAGCGGATATATCGAAGCCGAAGTGATCCCTGCCGAAACTGGACAGGAAACCGCTTACTTTATCCTCAAGA$ TTAAGCCTGTGGTCAGCACACAGCTCCTGCTCAACGGTAGCCTCGCTGAAGAGGAAATCATTATCAGAAGCGAAAA CTTTACCGATAACAAACTGGTCGGCAAACTGAATTGGGCTTCCCAAATCTACGCTGGCATCAAAGTGAAGCAACTG AGAGACAGACCCTTGTGACGCCGCCCCTAGCTCCAACTTTCTGGGAAGGTCTGCCGAACCCGTCCCGCCCCAGCCC $\tt GGTTCAATATCACCAACTGGCTGTGGTACATTAAGATTTTCATTATGATTGTGGGAGGCAATAAGATTGTCAGGAT$ $\tt GTACTCACCTGTCTCCATCCTCGACATTAAGCAAGGCCCTAAGGAACCCTTCAGGGATTACGTGGACAGATTCGCT$ AAGCTCCTGTGGAAGGGAGGGAGCCGTCGTGATTCAGGACAACTCCGACATTAAGGTCGTGCCCAGGAGAAAGG CTAAGATTATCGAACTGAATAAGAGAACCCAAGACTTTTGTGAAGTGCAACTGGGAATCCCTCACCCTGCTGGACT GAAGAAGAAAAGTCAGTGACAGTGGCCGCTATGAGAGTGAAAGAGACACAGATGAACTGGCCCAATCTGTGGAAG ${\tt TGGGGCACAATGATTCTGGGACTGGTCATCATTTGCTCCGCCTCCATTAAGGTCAGACAGCTCTGCAAACTGCTCA}$ $\tt GGGGTACAAAGGCTCTGACAGAGATTGTGACACTGACAGAGGAAGCCGAACTGGAACTGCTCATATGGAAGTTTGA$ CTCCCGCCTCGCCCTGAGACATATCGCCAGGGAACTGCATCCCGAGTTCTACAAAGACTGCGCTGCTGTCGAGCTC ${\tt GGGGCTCTAGCCTGGGGCAACTGCAACCTGCTCTGAAAACCGGATCAGAGGAACTGAAGTCCCTGTATAACACAAT}$ $\tt CGCTACCCTCTGGTGTGTGCATCAGGAGCTCTACAAATACAAAGTGGTCAAAATCAAACCCCTCGGCATTGCCCCT$ ACCAGAGCCAAAAGGAGAGTGGTCGAGAGAGAAAAAGGCTCACCGAAATCGTCCCACTCACCGAAGAGGCTGAGC TGGAGCTGGAGGAAAACAGAGAGATTCTGAGGGAACCCGTCCACGGAGTGTATAGAGTGCTCGCCGAAGCCATGAG CCAAGTCAACAATGCCAACATCATGATGCAGAGAGGCCAATTTCAAAGGCCTAAAGAGAATCATCAAACAAGAGGAA GAGGAGGTCGGCTTCCCCGTCAGGCCCCAGGTCCCACTGAGACCTATGACCTACAAAGGAGCCGTCGATCTGTCCT TCTTCAGACAGGGACCCAAAGAGCCTTTCAGAGACTATGTGGATAGGTTTTTCAAAACCCTCAGGGCTGAGCAAGC $\tt CTCACAGGAAGTGAAAAACTGGGAGAAAATCAGACTGAGACCTGGTGGCAAAAAGAAATACAAAATGAAACACATT$ $\tt GTGTGGGCCTCCAGGGAACTGGAAAGGTTTGCCTCCCAGTATGCCCTCGGCATCATCCTAGCCCAACCCGATAAGT$ AGGTGGCCGTCAGGACAATCTATACCGATAACGGAAGCCAATTTCACAAGCGCTACCGTCAAGGCTGCCTGGT GGGCTGATGTGAAACAGCTCACCGCAGTCGTCCAGAAAATCGCTACCGAAAGCATTGTGATATGGGGAAAGACGCC CAAGTTCAGACTGCCTATCGCTGCCGCCAGCAACGAGAACATGGAGACCATGGCTGCTtgaagatctgaattc

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C2 fragment

ggatccaccATGCTCGAGAGCAACACAGCCGCTAACAATACCGATTGCGTGTGGCTGAAAGCCCAGGAAGAGGAAG AAGTGGGATTTCCTGTGAGACCCCAAGTGCCTAGAGCCGGGAGGGCTATCCTCAACATTCCCACGAGGATTAGGCA AGGCCTTGAGAGAGCCCTCCTAGCCGCCGAATGGGATAGGATTCACCCTGTGCACGCTGGCCCTATCGCTCCCGGC CAAATGAGAGAGCCCAGGGGAAGCGATATCGCTGGCACAACCCTCAGGCCCATGACATATAAGGCCGCTATTGACC TCAGCTTGTTTCTGAAAGAGAAAGGCGGACTGGATGGCCTCATCTATAGCAAGAAAGCTGCTATGGAACAGGCTCC CGAAGACCAAAGCTCTCAGAGAGAGCCTTACAATGAGTGGACCCTGGAGGCTCCTGGAAGAGCTCAAGCACGAGGCT CAAGGCCAATGGACCTTCCAAATCTTTCAGGAACCCTTTAAGAATCTGAAAACCGGAAAGTATGCCAGAATGAGAG GCGCTCACACAAACTGGATGACAGATACCCTCCTGGTCCAGAATGCCAATCCCGATTGCAAGTCCATCCTCAAGGC ${\tt CAAGACCTGAATATGATGCTCAACACCGTCGGCGGACACCAATCCACCCTCCAGGAACAGATTGGCTGGATGACAA}$ ATAACCCTCCCATCCCTGTCGGAGAGATTTACAAAAGGTGGATTATCCTCGGCCTGACTAGAATCCCCCATCCCGC CGGCCTCAAGAAAAAGCAAAAGCGTCACCGTCCTGGATGTGGGAGACGCTTACTTCAGCGTCCCCTCGACGAAGGC ${\tt CAAAGGGAAACCTGGGAGGCTTGGTGGATGGAATACTGGCAGGCTACCTGGATTCCTGAGGGGGAGTTTGTGAATA}$ CCCCTCCCTCGTGTTTCCCGATTGGCAAAACTATACCCCTGGCCCTGGCACAAGGTATCCCCTCACCTTTGGATG TTTTACGCGGACGGAGCCGCCAACAGAGAGACAAAGCTCGGCCAAAACGTCCAGGGACAGATGGTGCATCAGCCTA TTAGCCCCAGGACCCTCAACGCTTGGGTCAAGGTCATCGAAGAGAAAGGCTTTAGCGACACCGAAGTGCATAACGT GATCAGAAACTCCTCGGCATTTGGGGATGCTCCGGCAAACTCATTTGCACAACCACTGTGCCTTGGAACAGCTCCT GGTCCAACCCAGCTGGCCATAACAAAGTGGGAAGCCTCCAGTATCTGGCTCTGAAGGCTCTGATTACGCCTAAGAA ${\tt AATCAAACCCCCTCTGCCTAGCGTTAAGACAATCATTGTGCATCTGAATGAGTCCGTGGAAATCAATTGCACAAGG}$ CCGATACAGGCAGCTCCAGCAAGGTCAGCCAAAACTATCCCATTGTGTCCAACTTTACCTCCACCACTGTGAAAGC $\tt CGCTTGTTGGTGGGCCAATATCAAACAGGAGTTTGGAATCCCTTACAATCCCCAAAGCCGAACATTCTATGTGGAT$ GAATCTGGCAGCTCGACTGTACCCATCTGAAAGGCAAAGTCATTCTGGTAGCCGTCCACGTCGGCTACAT ATCGATAAGGCTCAGGAAGACCACGAAGTCAGGGAAAGGATTAGGCGAGCCGCTCCCGCTGCTGAAGGCGTCGGCG CTGTCTCCCAGGATCTGGATAAGTACGGAGCCATCACCTCCACAAGCGGAACCCAACAGTCCCAGGGAACTGAAAC TGGCGTCGGCAACCCTCAGATTTTGGGAGAGTCCAGCGCTGTCCTCGGCTCCGGCTCCATCGTCATCTGGGGTAAA ACAGACTGATCAGCTGTAACACAAGCGTTATCACACAGGCTTGCCCTAAGATTAGCTTTGAGCCTATCCCTATCCA GAAAAGGAGTCCTGGACAGTGAATGACATTCAGAAAACAATTCTGAAAGCCCTCGGCCCCAGGCGCTACCCTGGAGG $\verb|AAAATATGACAGCATGTCAGGGAGTGGGAGGCCCTGGCCATAAGGCTAGAGTGTATTACAGAGACTCCAGGGACCC|$ ${\tt CATTTGGAAAGGCCCTGCCAAACTGCTCTGGAAAGGCGAAGGCGCTGTGGTCATCCAAGACATTAAGATTGGAGGCCGCTGTGGAAGGCCCTGTGGAAGGCCGCAAGACATTAAGATTGGAGGCCGAAGGCGCTGTGGTCATCCAAGACATTAAGATTGGAGGCCCTGTGGAAAGGCCGCTGTGGAAGGCCGCTGTGGTCATCCAAGACATTAAGATTGGAGGCCCTGTGGAAAGGCCGCTGTGGTCATCCAAGACATTAAGATTGGAGGCCCTGTGGAAAGGCCGCTGTGGTCATCCAAGACATTAAGATTGGAGGCCCTGTGGAAAGGCCGCTGTGGTCATCCAAGACATTAAGATTGGAGGCCCTGTGGAAAGGCCGCTGTGGTCATCCAAGACATTAAGATTGGAGGCCCTGTGGAAGACATTAAGATTGGAGGCCCTGTGGAAGACATTAAGATTGGAGGCCCTGTGGAAGACATTAAGATTGGAGGCCCTGTGGAAAGGCCGCTGTGGAAGACATTAAGATTTGGAGGCCCTGTGGAAAGGCCGCTGTGGAAAGGCCGCTGTGGAAAGACATTAAGATTTGGAGGCCCTGTGAAAGACATTAAGATTTGGAGGCCCTGTGAAAGACATTAAGATTTGGAAGACATTAAGATTTGGAAGACATTAAGATTTGGAAGACATTAAGATTTGGAAGACATTAAGATTTGGAAGACATTAAGATTTGGAAGACATTAAGATTTGGAAGACATTAAGATTAAGATTTGGAAGACATTAAGATTTGGAAGACATTAAGATTTGGAAGACATTAAGATTTGAAGATTAAGATTTGAAGATTAA$ CAACTGAAAGAAGCCCTCCTGGATACAGGAGCCGATGACACCGTCCTGGAAGATATCAATCTGCCTGGCAAGTGGG CTGTAGCGGAAAGGCTGCTATGGAAAACAGATGGCAAGTGATGATCGTCTGGCAAGTGGACAGGATGAAGATTAGG

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ACATGGAATAGCCTCGTGAAACACCATATGTATCTTATCTGTACCACGCCGTCCCCTGGAACTCCACCTGGAGCA ${ t ATAAGTCCTTCGAAGAGATTTGGAATAACATGACCTGGATTGAATGGCTGATTATCGCTATCGTCGTGGGACCAT$ TGTGTTTATCGAATACAAGAAACTGCTCAGGCAAAGGAAAATCGATAGGCTCATCGAAAGGCTCAACCCTGGCCTC ${ t CAATGAGTCCGAGGGAGACACCCCGGAATCAGATACCAATACAATGTGCTCCCCCAAGGCTGGAAGGGCTCCCCA$ GCCATTTTCCAAAGCTCCATGACCAAAATCCTCATGATGCAAAGGGGAAACTTTAAGGGACAGAAAAGGATTATCA AGTGCTTCAACTGTGGAAAGGAAGGCCATCTCGCTAGGAATTGCAGACCTCCCCTGGAGAGACTGAACCTGGATTG $\tt CTCCGAGGATAGCGACACCTCCGGCACACAGCAAAGCCAAGGCACAGAGACAGGAGTGGGACTCGTGGCTGTGCAT$ GTGGCCAGCGGATATATCGAAGCCGAAGTGATCCCTGCCGAAACTGGACAGGAAACCGCTTACTTTCTCCTCAAGA TTAAGCCTGTGGTCAGCACACCTCCTGCTCAACGGTAGCCTCGCTGAAGAGGGAAATCATTATCAGAAGCGAAAA $\tt CTTTACCAATAACAAACTGGTCGGCAAACTGAATTGGGCTTCCCAAATCTACCCTGGCATCAAAGTGAGGCAACTG$ AGAGACAGACCCTTTTGACGCCGCCCCTAGCTCCACCTTTCTGGGAAGGTCTGTCGAACCCGTCCCCCTCCAGCTC GGTTCAATATCACCAACTGGCTGTGGTACATTAAGATTTTCATTATGATTGTGGGAGGCAATAAGATTGTCAGGAT $\tt GTACCAACCTGTCTCCATCCTCGACATTAAGCAAGGCCCTAAGGAACCCTTCAGGGATTACGTGGACAGATTCGCT$ AAGCTCCTGTGGAAGGGAGAGGCCGTCGTGATTCAGGACAACTCCGACATTAAGGTCGTGCCCAGGAGAAAGG $\tt CTAAGATTATCGAACTGAATAAGAGAACCCAAGACTTTTGGGAAGCGCAACTGGGGAATCCCTCACCATGCTGGACT$ GAAAAAGAAAAAGTCCGTGACAGTGGCCGCTATGAGAGTGAAAGAGACACAGATGAACTGGCCCAATCTGTGGAAG TGGGGCACAATGATTCTGGGACTGGTCATCATTTGCTCCGCCTCCATTAAGGTCAAACAGCTCTGCAAACTGCTCA GGGGTGCAAAGGCTCTGATAGACATTGTGCCACTGACAGAGGAAGCCGAACTGGAACTGCTCATATGGAAGTTTGA CTCCCACCTCGCCCTGAGACATATCGCCAGGGAACTGCATCCCGAGTACTACAAAGACTGCGCTGCTGTCGAGCTC CTGGGACGCTCCAGCCTCAAGGAACTGCGAAGGGGATGGGAAGCCCTCAAGTATTTGTGGAACCTCCTGCAGTATT GGGGCTCTAGCCTGGAGCAACTGCAATCTGCTCTGAAAACCGGATCAGAGGAACTGAGGTCCCTGTTTAACACAGT CGCTACCCTCTGGTGTGTGCATCAGGAGCTCTACAAATACAAAGTGGTCAAAATCGAACCCCTCGGCATTGCCCCT ACCAAAGCCAAAAGGAGAGTGGTCCAGAGAGAGAGAAAAGGCTCACCGATATCGTCACACTCACCGAAGAGGCTGAGC TGGAGCTGGAGGAAAACAGAGAGATTCTGAAGGAACCCGTCCACGGAGTGTATAGAGTGCTCGCCGAAGCCATGAG CCAAGCCAACAATGCCAACATCATGATGCAGAGAGGGCAATTTCAGAGGGCCCAAAGAGAATCATCAAACAAGAGGAA GAGGGGGTCGGCTTCCCCGTCAGGCCTCAGGTCCCACTGAGACCTATGACCTACAAAGCAGCCATCGATCTGTCCT CTCACAGGAAGTGAAAAACTGGGAGAAAATCAGACTGAGATCTGGTGGCAAAAAGAAATACAAACTGAAACACATT $\tt GTGTGGGCCTCCAGGGAACTGGAAAGGTTTGCCTCCCAGTATGCCCTCGGCATCATCCTAGCCCAACCCGATAAGT$ AGGTGGCCCGTCAAGATAATCCATACCGATAACGGAAGCAATTTCACAAGCACTGCCGTCAAGGCTGCCTGGT GGGCTGATGTGAAACAGCTCACCGAAGTCGTTCAGAAAATCGCTACCGAAAGCATTGTGATATGGGGAAAGACACC CAAGTTCAGACAGCCTATCGCTGCCGCCAGCAACGAGAACATGGACGCCATGGCTGCTtgaagatctgaattc

INTERNATIONAL SEARCH REPORT

CLASSIFICATION OF SUBJECT MATTER

WO 99/41368 A. MAXYGEN INC. 19/8/99

Biotechnol Prog. Jan-Feb 2000. 16: 2-16.

A.

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International application No.

All

A11

PCT/AU01/00622

Int. Cl. 7: C07K 19/00; C12Q 1/68; C07K 2/00, 14/005, 14/15, 14/20, 14/435; C12N 15/09 According to International Patent Classification (IPC) or to both national classification and IPC FIELDS SEARCHED Minimum documentation searched (classification system followed by classification symbols) SEE ELECTRONIC DATABASES BELOW Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched SEE ELECTORNIC DATABASES BELOW Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) CA WPIDS MEDLINE: Combinatorial protein/peptide/polypeptide; gene/DNA shuffling; domain swapping; vaccine; synthetic protein/peptide polypeptide DOCUMENTS CONSIDERED TO BE RELEVANT C. Citation of document, with indication, where appropriate, of the relevant passages Relevant to claim No. Category* A11 WO 00/18906 A. MAXYGEN INC. 6/4/00 X A11 X WO 99/41402 A. MAXYGEN INC. 19/8/99 WO 99/41369 A. MAXYGEN INC. 19/8/99 All X

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"О"		y" document of particular relevance; the be considered to involve an inventive combined with one or more other succombination being obvious to a persent document member of the same patent.	e step when the document is ch documents, such on skilled in the art	
Date of the actu	nal completion of the international search	Date of mailing of the international search	j.	
1/8/01		7 Augu	11 2001	
Name and mail	ing address of the ISA/AU	Authorized officer		
PO BOX 200, V	VPATENT OFFICE WODEN ACT 2606, AUSTRALIA : pct@ipaustralia.gov.au	Gillian Allen		

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Facsimile No. (02) 6285 3929

INTERNATIONAL SEARCH REPORT

International application No.

PCT/AU01/00622

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International application No. PCT/AU01/00622

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•			EP 1056842

END OF ANNEX